SEQUENCE LISTING

<110> Galdes, Alphonse
Mahanthappa, Nagesh

<120> METHODS AND COMPOSITIONS FOR TREATING OR PREVENTING PERIPHERAL NEUROPATHIES

<130> BIV-052.02

<140> 09/435,733
<141> 1999-11-08

<160> 28

<170> PatentIn Ver. 2.0

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  1               5                  10                  15

tgc gct ctt tta gtc tcc tct ggg ctg act tgt gga cca ggc agg ggc   96
Cys Ala Leu Leu Val Ser Ser Gly Leu Thr Cys Gly Pro Gly Arg Gly
             20                  25                  30

att gga aaa agg agg cac ccc aaa aag ctg acc ccg tta gcc tat aag   144
Ile Gly Lys Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys
         35                  40                  45

cag ttt att ccc aat gtg gca gag aag acc cta ggg gcc agt gga aga   192
Gln Phe Ile Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Arg
     50                  55                  60

tat gaa ggg aag atc aca aga aac tcc gag aga ttt aaa gaa cta acc   240
Tyr Glu Gly Lys Ile Thr Arg Asn Ser Glu Arg Phe Lys Glu Leu Thr
 65                  70                  75                  80

cca aat tac aac cct gac att att ttt aag gat gaa gag aac acg gga   288
Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Gly
                 85                  90                  95

gct gac aga ctg atg act cag cgc tgc aag gac aag ctg aat gcc ctg   336
Ala Asp Arg Leu Met Thr Gln Arg Cys Lys Asp Lys Leu Asn Ala Leu
            100                 105                 110

gcg atc tcg gtg atg aac cag tgg ccc ggg gtg aag ctg cgg gtg acc   384
Ala Ile Ser Val Met Asn Gln Trp Pro Gly Val Lys Leu Arg Val Thr
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gag ggc tgg gac gag gat ggc cat cac tcc gag gaa tcg ctg cac tac   432
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gag ggt cgc gcc gtg gac atc acc acg tcg gat cgg gac cgc agc aag   480
Glu Gly Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Arg Ser Lys
145                 150                 155                 160

tac gga atg ctg gcc cgc ctc gcc gtc gag gcc ggc ttc gac tgg gtc   528
Tyr Gly Met Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val
                165                 170                 175

tac tac gag tcc aag gcg cac atc cac tgc tcc gtc aaa gca gaa aac   576
Tyr Tyr Glu Ser Lys Ala His Ile His Cys Ser Val Lys Ala Glu Asn
            180                 185                 190

tca gtg gca gcg aaa tca gga ggc tgc ttc cct ggc tca gcc aca gtg   624
Ser Val Ala Ala Lys Ser Gly Gly Cys Phe Pro Gly Ser Ala Thr Val
        195                 200                 205

cac ctg gag cat gga ggc acc aag ctg gtg aag gac ctg agc cct ggg   672
His Leu Glu His Gly Gly Thr Lys Leu Val Lys Asp Leu Ser Pro Gly
    210                 215                 220

gac cgc gtg ctg gct gct gac gcg gac ggc cgg ctg ctc tac agt gac   720
Asp Arg Val Leu Ala Ala Asp Ala Asp Gly Arg Leu Leu Tyr Ser Asp
225                 230                 235                 240

ttc ctc acc ttc ctc gac cgg atg gac agc tcc cga aag ctc ttc tac   768
Phe Leu Thr Phe Leu Asp Arg Met Asp Ser Ser Arg Lys Leu Phe Tyr
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gtc atc gag acg cgg cag ccc cgg gcc cgg ctg cta ctg acg gcg gcc   816
Val Ile Glu Thr Arg Gln Pro Arg Ala Arg Leu Leu Leu Thr Ala Ala
            260                 265                 270

cac ctg ctc ttt gtg gcc ccc cag cac aac cag tcg gag gcc aca ggg   864
His Leu Leu Phe Val Ala Pro Gln His Asn Gln Ser Glu Ala Thr Gly
        275                 280                 285

tcc acc agt ggc cag gcg ctc ttc gcc agc aac gtg aag cct ggc caa   912
Ser Thr Ser Gly Gln Ala Leu Phe Ala Ser Asn Val Lys Pro Gly Gln
    290                 295                 300

cgt gtc tat gtg ctg ggc gag ggc ggg cag cag ctg ctg ccg gcg tct   960
Arg Val Tyr Val Leu Gly Glu Gly Gly Gln Gln Leu Leu Pro Ala Ser
305                 310                 315                 320

gtc cac agc gtc tca ttg cgg gag gag gcg tcc gga gcc tac gcc cca   1008
Val His Ser Val Ser Leu Arg Glu Glu Ala Ser Gly Ala Tyr Ala Pro
                325                 330                 335

ctc acc gcc cag ggc acc atc ctc atc aac cgg gtg ttg gcc tcc tgc   1056
Leu Thr Ala Gln Gly Thr Ile Leu Ile Asn Arg Val Leu Ala Ser Cys
            340                 345                 350
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tac gcc gtc atc gag gag cac agt tgg gcc cat tgg gcc ttc gca cca   1104
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ttc cgc ttg gct cag ggg ctg ctg gcc gcc ctc tgc cca gat ggg gcc   1152
Phe Arg Leu Ala Gln Gly Leu Leu Ala Ala Leu Cys Pro Asp Gly Ala
    370                 375                 380

atc cct act gcc gcc acc acc acc act ggc atc cat tgg tac tca cgg   1200
Ile Pro Thr Ala Ala Thr Thr Thr Thr Gly Ile His Trp Tyr Ser Arg
385                 390                 395                 400

ctc ctc tac cgc atc ggc agc tgg gtg ctg gat ggt gac gcg ctg cat   1248
Leu Leu Tyr Arg Ile Gly Ser Trp Val Leu Asp Gly Asp Ala Leu His
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ccg ctg ggc atg gtg gca ccg gcc agc tg                            1277
Pro Leu Gly Met Val Ala Pro Ala Ser
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  1               5                  10                  15

gca cta tct gcc cag agc tgc ggg ccg ggc cga gga ccg gtt ggc cgg   96
Ala Leu Ser Ala Gln Ser Cys Gly Pro Gly Arg Gly Pro Val Gly Arg
             20                  25                  30

cgg cgt tat gtg cgc aag caa ctt gtg cct ctg cta tac aag cag ttt   144
Arg Arg Tyr Val Arg Lys Gln Leu Val Pro Leu Leu Tyr Lys Gln Phe
         35                  40                  45

gtg ccc agt atg ccc gag cgg acc ctg ggc gcg agt ggg cca gcg gag   192
Val Pro Ser Met Pro Glu Arg Thr Leu Gly Ala Ser Gly Pro Ala Glu
     50                  55                  60

ggg agg gta aca agg ggg tcg gag cgc ttc cgg gac ctc gta ccc aac   240
Gly Arg Val Thr Arg Gly Ser Glu Arg Phe Arg Asp Leu Val Pro Asn
 65                  70                  75                  80

tac aac ccc gac ata atc ttc aag gat gag gag aac agc ggc gca gac   288
Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Ser Gly Ala Asp
                 85                  90                  95

cgc ctg atg aca gag cgt tgc aaa gag cgg gtg aac gct cta gcc atc   336
Arg Leu Met Thr Glu Arg Cys Lys Glu Arg Val Asn Ala Leu Ala Ile
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            100                 105                 110

gcg gtg atg aac atg tgg ccc gga gta cgc cta cgt gtg act gaa ggc   384
Ala Val Met Asn Met Trp Pro Gly Val Arg Leu Arg Val Thr Glu Gly
        115                 120                 125

tgg gac gag gac ggc cac cac gca cag gat tca ctc cac tac gaa ggc   432
Trp Asp Glu Asp Gly His His Ala Gln Asp Ser Leu His Tyr Glu Gly
    130                 135                 140

cgt gcc ttg gac atc acc acg tct gac cgt gac cgt aat aag tat ggt   480
Arg Ala Leu Asp Ile Thr Thr Ser Asp Arg Asp Arg Asn Lys Tyr Gly
145                 150                 155                 160

ttg ttg gcg cgc cta gct gtg gaa gcc gga ttc gac tgg gtc tac tac   528
Leu Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val Tyr Tyr
                165                 170                 175

gag tcc cgc aac cac atc cac gta tcg gtc aaa gct gat aac tca ctg   576
Glu Ser Arg Asn His Ile His Val Ser Val Lys Ala Asp Asn Ser Leu
            180                 185                 190

gcg gtc cga gcc gga ggc tgc ttt ccg gga aat gcc acg gtg cgc ttg   624
Ala Val Arg Ala Gly Gly Cys Phe Pro Gly Asn Ala Thr Val Arg Leu
        195                 200                 205

cgg agc ggc gaa cgg aag ggg ctg agg gaa cta cat cgt ggt gac tgg   672
Arg Ser Gly Glu Arg Lys Gly Leu Arg Glu Leu His Arg Gly Asp Trp
    210                 215                 220

gta ctg gcc gct gat gca gcg ggc cga gtg gta ccc acg cca gtg ctg   720
Val Leu Ala Ala Asp Ala Ala Gly Arg Val Val Pro Thr Pro Val Leu
225                 230                 235                 240

ctc ttc ctg gac cgg gat ctg cag cgc cgc gcc tcg ttc gtg gct gtg   768
Leu Phe Leu Asp Arg Asp Leu Gln Arg Arg Ala Ser Phe Val Ala Val
                245                 250                 255

gag acc gag cgg cct ccg cgc aaa ctg ttg ctc aca ccc tgg cat ctg   816
Glu Thr Glu Arg Pro Pro Arg Lys Leu Leu Leu Thr Pro Trp His Leu
            260                 265                 270

gtg ttc gct gct cgc ggg cca gcg cct gct cca ggt gac ttt gca ccg   864
Val Phe Ala Ala Arg Gly Pro Ala Pro Ala Pro Gly Asp Phe Ala Pro
        275                 280                 285

gtg ttc gcg cgc cgc tta cgt gct ggc gac tcg gtg ctg gct ccc ggc   912
Val Phe Ala Arg Arg Leu Arg Ala Gly Asp Ser Val Leu Ala Pro Gly
    290                 295                 300

ggg gac gcg ctc cag ccg gcg cgc gta gcc cgc gtg gcg cgc gag gaa   960
Gly Asp Ala Leu Gln Pro Ala Arg Val Ala Arg Val Ala Arg Glu Glu
305                 310                 315                 320

gcc gtg ggc gtg ttc gca ccg ctc act gcg cac ggg acg ctg ctg gtc  1008
Ala Val Gly Val Phe Ala Pro Leu Thr Ala His Gly Thr Leu Leu Val
                325                 330                 335
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aac gac gtc ctc gcc tcc tgc tac gcg gtt cta gag agt cac cag tgg   1056
Asn Asp Val Leu Ala Ser Cys Tyr Ala Val Leu Glu Ser His Gln Trp
            340                 345                 350

gcc cac cgc gcc ttc gcc cct ttg cgg ctg ctg cac gcg ctc ggg gct   1104
Ala His Arg Ala Phe Ala Pro Leu Arg Leu Leu His Ala Leu Gly Ala
        355                 360                 365

ctg ctc cct ggg ggt gca gtc cag ccg act ggc atg cat tgg tac tct   1152
Leu Leu Pro Gly Gly Ala Val Gln Pro Thr Gly Met His Trp Tyr Ser
    370                 375                 380

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  1               5                  10                  15

ctg ctg ctg ctt ctg gtg ccg gcg gcg cgg ggc tgc ggg ccg ggc cgg   96
Leu Leu Leu Leu Leu Val Pro Ala Ala Arg Gly Cys Gly Pro Gly Arg
             20                  25                  30

gtg gtg ggc agc cgc cgg agg ccg cct cgc aag ctc gtg cct ctt gcc   144
Val Val Gly Ser Arg Arg Arg Pro Pro Arg Lys Leu Val Pro Leu Ala
         35                  40                  45

tac aag cag ttc agc ccc aac gtg ccg gag aag acc ctg ggc gcc agc   192
Tyr Lys Gln Phe Ser Pro Asn Val Pro Glu Lys Thr Leu Gly Ala Ser
     50                  55                  60

ggg cgc tac gaa ggc aag atc gcg cgc agc tct gag cgc ttc aaa gag   240
Gly Arg Tyr Glu Gly Lys Ile Ala Arg Ser Ser Glu Arg Phe Lys Glu
 65                  70                  75                  80

ctc acc ccc aac tac aat ccc gac atc atc ttc aag gac gag gag aac   288
Leu Thr Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn
                85                  90                  95

acg ggt gcc gac cgc ctc atg acc cag cgc tgc aag gac cgt ctg aac   336
Thr Gly Ala Asp Arg Leu Met Thr Gln Arg Cys Lys Asp Arg Leu Asn
            100                 105                 110

tca ctg gcc atc tct gtc atg aac cag tgg cct ggt gtg aaa ctg cgg   384
Ser Leu Ala Ile Ser Val Met Asn Gln Trp Pro Gly Val Lys Leu Arg
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        115                 120                 125

gtg acc gaa ggc cgg gat gaa gat ggc cat cac tca gag gag tct tta   432
Val Thr Glu Gly Arg Asp Glu Asp Gly His His Ser Glu Glu Ser Leu
    130                 135                 140

cac tat gag ggc cgc gcg gtg gat atc acc acc tca gac cgt gac cga   480
His Tyr Glu Gly Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Arg
145                 150                 155                 160

aat aag tat gga ctg ctg gcg cgc tta gca gtg gag gcc ggc ttc gac   528
Asn Lys Tyr Gly Leu Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp
                165                 170                 175

tgg gtg tat tac gag tcc aag gcc cac gtg cat tgc tct gtc aag tct   576
Trp Val Tyr Tyr Glu Ser Lys Ala His Val His Cys Ser Val Lys Ser
            180                 185                 190

gag cat tcg gcc gct gcc aag aca ggt ggc tgc ttt cct gcc gga gcc   624
Glu His Ser Ala Ala Ala Lys Thr Gly Gly Cys Phe Pro Ala Gly Ala
        195                 200                 205

cag gtg cgc cta gag aac ggg gag cgt gtg gcc ctg tca gct gta aag   672
Gln Val Arg Leu Glu Asn Gly Glu Arg Val Ala Leu Ser Ala Val Lys
    210                 215                 220

cca gga gac cgg gtg ctg gcc atg ggg gag gat ggg acc ccc acc ttc   720
Pro Gly Asp Arg Val Leu Ala Met Gly Glu Asp Gly Thr Pro Thr Phe
225                 230                 235                 240

agt gat gtg ctt att ttc ctg gac cgc gag cca aac cgg ctg aga gct   768
Ser Asp Val Leu Ile Phe Leu Asp Arg Glu Pro Asn Arg Leu Arg Ala
                245                 250                 255

ttc cag gtc atc gag act cag gat cct ccg cgt cgg ctg gcg ctc acg   816
Phe Gln Val Ile Glu Thr Gln Asp Pro Pro Arg Arg Leu Ala Leu Thr
            260                 265                 270

cct gcc cac ctg ctc ttc att gcg gac aat cat aca gaa cca gca gcc   864
Pro Ala His Leu Leu Phe Ile Ala Asp Asn His Thr Glu Pro Ala Ala
        275                 280                 285

cac ttc cgg gcc aca ttt gcc agc cat gtg caa cca ggc caa tat gtg   912
His Phe Arg Ala Thr Phe Ala Ser His Val Gln Pro Gly Gln Tyr Val
    290                 295                 300

ctg gta tca ggg gta cca ggc ctc cag cct gct cgg gtg gca gct gtc   960
Leu Val Ser Gly Val Pro Gly Leu Gln Pro Ala Arg Val Ala Ala Val
305                 310                 315                 320

tcc acc cac gtg gcc ctt ggg tcc tat gct cct ctc aca agg cat ggg  1008
Ser Thr His Val Ala Leu Gly Ser Tyr Ala Pro Leu Thr Arg His Gly
                325                 330                 335

aca ctt gtg gtg gag gat gtg gtg gcc tcc tgc ttt gca gct gtg gct  1056
Thr Leu Val Val Glu Asp Val Val Ala Ser Cys Phe Ala Ala Val Ala
            340                 345                 350
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gac cac cat ctg gct cag ttg gcc ttc tgg ccc ctg cga ctg ttt ccc   1104
Asp His His Leu Ala Gln Leu Ala Phe Trp Pro Leu Arg Leu Phe Pro
        355                 360                 365

agt ttg gca tgg ggc agc tgg acc cca agt gag ggt gtt cac tcc tac   1152
Ser Leu Ala Trp Gly Ser Trp Thr Pro Ser Glu Gly Val His Ser Tyr
    370                 375                 380

cct cag atg ctc tac cgc ctg ggg cgt ctc ttg cta gaa gag agc acc   1200
Pro Gln Met Leu Tyr Arg Leu Gly Arg Leu Leu Leu Glu Glu Ser Thr
385                 390                 395                 400

ttc cat cca ctg ggc atg tct ggg gca gga agc tgaagggact ctaaccactg 1253
Phe His Pro Leu Gly Met Ser Gly Ala Gly Ser
                405                 410

ccctcctgga actgctgtgc gtggatcc                                    1281


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<213> mouse Shh

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  1               5                  10                  15

ctg ctg gtg tgc ccc ggg ctg gcc tgt ggg ccc ggc agg ggg ttt gga   96
Leu Leu Val Cys Pro Gly Leu Ala Cys Gly Pro Gly Arg Gly Phe Gly
             20                  25                  30

aag agg cgg cac ccc aaa aag ctg acc cct tta gcc tac aag cag ttt   144
Lys Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys Gln Phe
         35                  40                  45

att ccc aac gta gcc gag aag acc cta ggg gcc agc ggc aga tat gaa   192
Ile Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Arg Tyr Glu
     50                  55                  60

ggg aag atc aca aga aac tcc gaa cga ttt aag gaa ctc acc ccc aat   240
Gly Lys Ile Thr Arg Asn Ser Glu Arg Phe Lys Glu Leu Thr Pro Asn
 65                  70                  75                  80

tac aac ccc gac atc ata ttt aag gat gag gaa aac acg gga gca gac   288
Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Gly Ala Asp
                 85                  90                  95

cgg ctg atg act cag agg tgc aaa gac aag tta aat gcc ttg gcc atc   336
Arg Leu Met Thr Gln Arg Cys Lys Asp Lys Leu Asn Ala Leu Ala Ile
            100                 105                 110
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tct gtg atg aac cag tgg cct gga gtg agg ctg cga gtg acc gag ggc   384
Ser Val Met Asn Gln Trp Pro Gly Val Arg Leu Arg Val Thr Glu Gly
        115                 120                 125

tgg gat gag gac ggc cat cat tca gag gag tct cta cac tat gag ggt   432
Trp Asp Glu Asp Gly His His Ser Glu Glu Ser Leu His Tyr Glu Gly
    130                 135                 140

cga gca gtg gac atc acc acg tcc gac cgg gac cgc agc aag tac ggc   480
Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Arg Ser Lys Tyr Gly
145                 150                 155                 160

atg ctg gct cgc ctg gct gtg gaa gca ggt ttc gac tgg gtc tac tat   528
Met Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val Tyr Tyr
                165                 170                 175

gaa tcc aaa gct cac atc cac tgt tct gtg aaa gca gag aac tcc gtg   576
Glu Ser Lys Ala His Ile His Cys Ser Val Lys Ala Glu Asn Ser Val
            180                 185                 190

gcg gcc aaa tcc ggc ggc tgt ttc ccg gga tcc gcc acc gtg cac ctg   624
Ala Ala Lys Ser Gly Gly Cys Phe Pro Gly Ser Ala Thr Val His Leu
        195                 200                 205

gag cag ggc ggc acc aag ctg gtg aag gac tta cgt ccc gga gac cgc   672
Glu Gln Gly Gly Thr Lys Leu Val Lys Asp Leu Arg Pro Gly Asp Arg
    210                 215                 220

gtg ctg gcg gct gac gac cag ggc cgg ctg ctg tac agc gac ttc ctc   720
Val Leu Ala Ala Asp Asp Gln Gly Arg Leu Leu Tyr Ser Asp Phe Leu
225                 230                 235                 240

acc ttc ctg gac cgc gac gaa ggc gcc aag aag gtc ttc tac gtg atc   768
Thr Phe Leu Asp Arg Asp Glu Gly Ala Lys Lys Val Phe Tyr Val Ile
                245                 250                 255

gag acg ctg gag ccg cgc gag cgc ctg ctg ctc acc gcc gcg cac ctg   816
Glu Thr Leu Glu Pro Arg Glu Arg Leu Leu Leu Thr Ala Ala His Leu
            260                 265                 270

ctc ttc gtg gcg ccg cac aac gac tcg ggg ccc acg ccc ggg cca agc   864
Leu Phe Val Ala Pro His Asn Asp Ser Gly Pro Thr Pro Gly Pro Ser
        275                 280                 285

gcg ctc ttt gcc agc cgc gtg cgc ccc ggg cag cgc gtg tac gtg gtg   912
Ala Leu Phe Ala Ser Arg Val Arg Pro Gly Gln Arg Val Tyr Val Val
    290                 295                 300

gct gaa cgc ggc ggg gac cgc cgg ctg ctg ccc gcc gcg gtg cac agc   960
Ala Glu Arg Gly Gly Asp Arg Arg Leu Leu Pro Ala Ala Val His Ser
305                 310                 315                 320

gtg acg ctg cga gag gag gag gcg ggc gcg tac gcg ccg ctc acg gcg   1008
Val Thr Leu Arg Glu Glu Glu Ala Gly Ala Tyr Ala Pro Leu Thr Ala
                325                 330                 335
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cac ggc acc att ctc atc aac cgg gtg ctc gcc tcg tgc tac gct gtc   1056
His Gly Thr Ile Leu Ile Asn Arg Val Leu Ala Ser Cys Tyr Ala Val
            340                 345                 350

atc gag gag cac agc tgg gca cac cgg gcc ttc gcg cct ttc cgc ctg   1104
Ile Glu Glu His Ser Trp Ala His Arg Ala Phe Ala Pro Phe Arg Leu
        355                 360                 365

gcg cac gcg ctg ctg gcc gcg ctg gca ccc gcc cgc acg gac ggc ggg   1152
Ala His Ala Leu Leu Ala Ala Leu Ala Pro Ala Arg Thr Asp Gly Gly
    370                 375                 380

ggc ggg ggc agc atc cct gca gcg caa tct gca acg gaa gcg agg ggc   1200
Gly Gly Gly Ser Ile Pro Ala Ala Gln Ser Ala Thr Glu Ala Arg Gly
385                 390                 395                 400

gcg gag ccg act gcg ggc atc cac tgg tac tcg cag ctg ctc tac cac   1248
Ala Glu Pro Thr Ala Gly Ile His Trp Tyr Ser Gln Leu Leu Tyr His
                405                 410                 415

att ggc acc tgg ctg ttg gac agc gag acc atg cat ccc ttg gga atg   1296
Ile Gly Thr Trp Leu Leu Asp Ser Glu Thr Met His Pro Leu Gly Met
            420                 425                 430

gcg gtc aag tcc agc tg                                           1313
Ala Val Lys Ser Ser
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Met Arg Leu Leu Thr Arg Val Leu Leu Val Ser Leu Leu Thr Leu Ser
  1               5                  10                  15

ttg gtg gtg tcc gga ctg gcc tgc ggt cct ggc aga ggc tac ggc aga   96
Leu Val Val Ser Gly Leu Ala Cys Gly Pro Gly Arg Gly Tyr Gly Arg
             20                  25                  30

aga aga cat ccg aag aag ctg aca cct ctc gcc tac aag cag ttc ata   144
Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys Gln Phe Ile
         35                  40                  45

cct aat gtc gcg gag aag acc tta ggg gcc agc ggc aga tac gag ggc   192
Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Arg Tyr Glu Gly
     50                  55                  60

aag ata acg cgc aat tcg gag aga ttt aaa gaa ctt act cca aat tac   240
Lys Ile Thr Arg Asn Ser Glu Arg Phe Lys Glu Leu Thr Pro Asn Tyr
 65                  70                  75                  80
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aat ccc gac att atc ttt aag gat gag gag aac acg gga gcg gac agg   288
Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Gly Ala Asp Arg
                 85                  90                  95

ctc atg aca cag aga tgc aaa gac aag ctg aac tcg ctg gcc atc tct   336
Leu Met Thr Gln Arg Cys Lys Asp Lys Leu Asn Ser Leu Ala Ile Ser
            100                 105                 110

gta atg aac cac tgg cca ggg gtt aag ctg cgt gtg aca gag ggc tgg   384
Val Met Asn His Trp Pro Gly Val Lys Leu Arg Val Thr Glu Gly Trp
        115                 120                 125

gat gag gac ggt cac cat ttt gaa gaa tca ctc cac tac gag gga aga   432
Asp Glu Asp Gly His His Phe Glu Glu Ser Leu His Tyr Glu Gly Arg
    130                 135                 140

gct gtt gat att acc acc tct gac cga gac aag agc aaa tac ggg aca   480
Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Lys Ser Lys Tyr Gly Thr
145                 150                 155                 160

ctg tct cgc cta gct gtg gag gct gga ttt gac tgg gtc tat tac gag   528
Leu Ser Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val Tyr Tyr Glu
                165                 170                 175

tcc aaa gcc cac att cat tgc tct gtc aaa gca gaa aat tcg gtt gct   576
Ser Lys Ala His Ile His Cys Ser Val Lys Ala Glu Asn Ser Val Ala
            180                 185                 190

gcg aaa tct ggg ggc tgt ttc cca ggt tcg gct ctg gtc tcg ctc cag   624
Ala Lys Ser Gly Gly Cys Phe Pro Gly Ser Ala Leu Val Ser Leu Gln
        195                 200                 205

gac gga gga cag aag gcc gtg aag gac ctg aac ccc gga gac aag gtg   672
Asp Gly Gly Gln Lys Ala Val Lys Asp Leu Asn Pro Gly Asp Lys Val
    210                 215                 220

ctg gcg gca gac agc gcg gga aac ctg gtg ttc agc gac ttc atc atg   720
Leu Ala Ala Asp Ser Ala Gly Asn Leu Val Phe Ser Asp Phe Ile Met
225                 230                 235                 240

ttc aca gac cga gac tcc acg acg cga cgt gtg ttt tac gtc ata gaa   768
Phe Thr Asp Arg Asp Ser Thr Thr Arg Arg Val Phe Tyr Val Ile Glu
                245                 250                 255

acg caa gaa ccc gtt gaa aag atc acc ctc acc gcc gct cac ctc ctt   816
Thr Gln Glu Pro Val Glu Lys Ile Thr Leu Thr Ala Ala His Leu Leu
            260                 265                 270

ttt gtc ctc gac aac tca acg gaa gat ctc cac acc atg acc gcc gcg   864
Phe Val Leu Asp Asn Ser Thr Glu Asp Leu His Thr Met Thr Ala Ala
        275                 280                 285

tat gcc agc agt gtc aga gcc gga caa aag gtg atg gtt gtt gat gat   912
Tyr Ala Ser Ser Val Arg Ala Gly Gln Lys Val Met Val Val Asp Asp
    290                 295                 300
```

```
agc ggt cag ctt aaa tct gtc atc gtg cag cgg ata tac acg gag gag   960
Ser Gly Gln Leu Lys Ser Val Ile Val Gln Arg Ile Tyr Thr Glu Glu
305                 310                 315                 320

cag cgg ggc tcg ttc gca cca gtg act gca cat ggg acc att gtg gtc   1008
Gln Arg Gly Ser Phe Ala Pro Val Thr Ala His Gly Thr Ile Val Val
                325                 330                 335

gac aga ata ctg gcg tcc tgt tac gcc gta ata gag gac cag ggg ctt   1056
Asp Arg Ile Leu Ala Ser Cys Tyr Ala Val Ile Glu Asp Gln Gly Leu
            340                 345                 350

gcg cat ttg gcc ttc gcg ccc gcc agg ctc tat tat tac gtg tca tca   1104
Ala His Leu Ala Phe Ala Pro Ala Arg Leu Tyr Tyr Tyr Val Ser Ser
        355                 360                 365

ttc ctg tcc ccc aaa act cca gca gtc ggt cca atg cga ctt tac aac   1152
Phe Leu Ser Pro Lys Thr Pro Ala Val Gly Pro Met Arg Leu Tyr Asn
    370                 375                 380

agg agg ggg tcc act ggt act cca ggc tcc tgt cat caa atg gga acg   1200
Arg Arg Gly Ser Thr Gly Thr Pro Gly Ser Cys His Gln Met Gly Thr
385                 390                 395                 400

tgg ctt ttg gac agc aac atg ctt cat cct ttg ggg atg tca gta aac   1248
Trp Leu Leu Asp Ser Asn Met Leu His Pro Leu Gly Met Ser Val Asn
                405                 410                 415

tca agc tg                                                       1256
Ser Ser
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<210> 6
<211> 1425
<212> DNA
<213> human Shh

<220>
<221> CDS
<222> (1)..(1425)

<220>
<223> "nnn" encoding "Xaa" at position 1387-1389 may be a, t, c, g, other or unknown

<400> 6

```
atg ctg ctg ctg gcg aga tgt ctg ctg cta gtc ctc gtc tcc tcg ctg   48
Met Leu Leu Leu Ala Arg Cys Leu Leu Leu Val Leu Val Ser Ser Leu
  1               5                  10                  15

ctg gta tgc tcg gga ctg gcg tgc gga ccg ggc agg ggg ttc ggg aag   96
Leu Val Cys Ser Gly Leu Ala Cys Gly Pro Gly Arg Gly Phe Gly Lys
            20                  25                  30

agg agg cac ccc aaa aag ctg acc cct tta gcc tac aag cag ttt atc   144
Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys Gln Phe Ile
        35                  40                  45
```

```
ccc aat gtg gcc gag aag acc cta ggc gcc agc gga agg tat gaa ggg   192
Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Arg Tyr Glu Gly
     50                  55                  60

aag atc tcc aga aac tcc gag cga ttt aag gaa ctc acc ccc aat tac   240
Lys Ile Ser Arg Asn Ser Glu Arg Phe Lys Glu Leu Thr Pro Asn Tyr
 65                  70                  75                  80

aac ccc gac atc ata ttt aag gat gaa gaa aac acc gga gcg gac agg   288
Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Gly Ala Asp Arg
                85                  90                  95

ctg atg act cag agg tgt aag gac aag ttg aac gct ttg gcc atc tcg   336
Leu Met Thr Gln Arg Cys Lys Asp Lys Leu Asn Ala Leu Ala Ile Ser
            100                 105                 110

gtg atg aac cag tgg cca gga gtg aaa ctg cgg gtg acc gag ggc tgg   384
Val Met Asn Gln Trp Pro Gly Val Lys Leu Arg Val Thr Glu Gly Trp
        115                 120                 125

gac gaa gat ggc cac cac tca gag gag tct ctg cac tac gag ggc cgc   432
Asp Glu Asp Gly His His Ser Glu Glu Ser Leu His Tyr Glu Gly Arg
    130                 135                 140

gca gtg gac atc acc acg tct gac cgc gac cgc agc aag tac ggc atg   480
Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Arg Ser Lys Tyr Gly Met
145                 150                 155                 160

ctg gcc cgc ctg gcg gtg gag gcc ggc ttc gac tgg gtg tac tac gag   528
Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val Tyr Tyr Glu
                165                 170                 175

tcc aag gca cat atc cac tgc tcg gtg aaa gca gag aac tcg gtg gcg   576
Ser Lys Ala His Ile His Cys Ser Val Lys Ala Glu Asn Ser Val Ala
            180                 185                 190

gcc aaa tcg gga ggc tgc ttc ccg ggc tcg gcc acg gtg cac ctg gag   624
Ala Lys Ser Gly Gly Cys Phe Pro Gly Ser Ala Thr Val His Leu Glu
        195                 200                 205

cag ggc ggc acc aag ctg gtg aag gac ctg agc ccc ggg gac cgc gtg   672
Gln Gly Gly Thr Lys Leu Val Lys Asp Leu Ser Pro Gly Asp Arg Val
    210                 215                 220

ctg gcg gcg gac gac cag ggc cgg ctg ctc tac agc gac ttc ctc act   720
Leu Ala Ala Asp Asp Gln Gly Arg Leu Leu Tyr Ser Asp Phe Leu Thr
225                 230                 235                 240

ttc ctg gac cgc gac gac ggc gcc aag aag gtc ttc tac gtg atc gag   768
Phe Leu Asp Arg Asp Asp Gly Ala Lys Lys Val Phe Tyr Val Ile Glu
                245                 250                 255

acg cgg gag ccg cgc gag cgc ctg ctg ctc acc gcc gcg cac ctg ctc   816
Thr Arg Glu Pro Arg Glu Arg Leu Leu Leu Thr Ala Ala His Leu Leu
            260                 265                 270

ttt gtg gcg ccg cac aac gac tcg gcc acc ggg gag ccc gag gcg tcc   864
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```
Phe Val Ala Pro His Asn Asp Ser Ala Thr Gly Glu Pro Glu Ala Ser
        275                 280                 285

tcg ggc tcg ggg ccg cct tcc ggg ggc gca ctg ggg cct cgg gcg ctg   912
Ser Gly Ser Gly Pro Pro Ser Gly Gly Ala Leu Gly Pro Arg Ala Leu
    290                 295                 300

ttc gcc agc cgc gtg cgc ccg ggc cag cgc gtg tac gtg gtg gcc gag   960
Phe Ala Ser Arg Val Arg Pro Gly Gln Arg Val Tyr Val Val Ala Glu
305                 310                 315                 320

cgt gac ggg gac cgc cgg ctc ctg ccc gcc gct gtg cac agc gtg acc   1008
Arg Asp Gly Asp Arg Arg Leu Leu Pro Ala Ala Val His Ser Val Thr
                325                 330                 335

cta agc gag gag gcc gcg ggc gcc tac gcg ccg ctc acg gcc cag ggc   1056
Leu Ser Glu Glu Ala Ala Gly Ala Tyr Ala Pro Leu Thr Ala Gln Gly
            340                 345                 350

acc att ctc atc aac cgg gtg ctg gcc tcg tgc tac gcg gtc atc gag   1104
Thr Ile Leu Ile Asn Arg Val Leu Ala Ser Cys Tyr Ala Val Ile Glu
        355                 360                 365

gag cac agc tgg gcg cac cgg gcc ttc gcg ccc ttc cgc ctg gcg cac   1152
Glu His Ser Trp Ala His Arg Ala Phe Ala Pro Phe Arg Leu Ala His
    370                 375                 380

gcg ctc ctg gct gca ctg gcg ccc gcg cgc acg gac cgc ggc ggg gac   1200
Ala Leu Leu Ala Ala Leu Ala Pro Ala Arg Thr Asp Arg Gly Gly Asp
385                 390                 395                 400

agc ggc ggc ggg gac cgc ggg ggc ggc ggc ggc aga gta gcc cta acc   1248
Ser Gly Gly Gly Asp Arg Gly Gly Gly Gly Gly Arg Val Ala Leu Thr
                405                 410                 415

gct cca ggt gct gcc gac gct ccg ggt gcg ggg gcc acc gcg ggc atc   1296
Ala Pro Gly Ala Ala Asp Ala Pro Gly Ala Gly Ala Thr Ala Gly Ile
            420                 425                 430

cac tgg tac tcg cag ctg ctc tac caa ata ggc acc tgg ctc ctg gac   1344
His Trp Tyr Ser Gln Leu Leu Tyr Gln Ile Gly Thr Trp Leu Leu Asp
        435                 440                 445

agc gag gcc ctg cac ccg ctg ggc atg gcg gtc aag tcc agc nnn agc   1392
Ser Glu Ala Leu His Pro Leu Gly Met Ala Val Lys Ser Ser Xaa Ser
    450                 455                 460

cgg ggg gcc ggg gga ggg gcg cgg gag ggg gcc                       1425
Arg Gly Ala Gly Gly Gly Ala Arg Glu Gly Ala
465                 470                 475
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<210> 7
<211> 1622
<212> DNA
<213> human Ihh

<220>

<221> CDS
<222> (51)..(1283)

<400> 7
catcagccca ccaggagacc tcgcccgccg ctcccccggg ctccccggcc atg tct 56
Met Ser
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ccc gcc cgg ctc cgg ccc cga ctg cac ttc tgc ctg gtc ctg ttg ctg 104
Pro Ala Arg Leu Arg Pro Arg Leu His Phe Cys Leu Val Leu Leu Leu
5 10 15

ctg ctg gtg gtg ccc gcg gca tgg ggc tgc ggg ccg ggt cgg gtg gtg 152
Leu Leu Val Val Pro Ala Ala Trp Gly Cys Gly Pro Gly Arg Val Val
20 25 30

ggc agc cgc cgg cga ccg cca cgc aaa ctc gtg ccg ctc gcc tac aag 200
Gly Ser Arg Arg Arg Pro Pro Arg Lys Leu Val Pro Leu Ala Tyr Lys
35 40 45 50

cag ttc agc ccc aat gtg ccc gag aag acc ctg ggc gcc agc gga cgc 248
Gln Phe Ser Pro Asn Val Pro Glu Lys Thr Leu Gly Ala Ser Gly Arg
55 60 65

tat gaa ggc aag atc gct cgc agc tcc gag cgc ttc aag gag ctc acc 296
Tyr Glu Gly Lys Ile Ala Arg Ser Ser Glu Arg Phe Lys Glu Leu Thr
70 75 80

ccc aat tac aat cca gac atc atc ttc aag gac gag gag aac aca ggc 344
Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Gly
85 90 95

gcc gac cgc ctc atg acc cag cgc tgc aag gac cgc ctg aac tcg ctg 392
Ala Asp Arg Leu Met Thr Gln Arg Cys Lys Asp Arg Leu Asn Ser Leu
100 105 110

gct atc tcg gtg atg aac cag tgg ccc ggt gtg aag ctg cgg gtg acc 440
Ala Ile Ser Val Met Asn Gln Trp Pro Gly Val Lys Leu Arg Val Thr
115 120 125 130

gag ggc tgg gac gag gac ggc cac cac tca gag gag tcc ctg cat tat 488
Glu Gly Trp Asp Glu Asp Gly His His Ser Glu Glu Ser Leu His Tyr
135 140 145

gag ggc cgc gcg gtg gac atc acc aca tca gac cgc gac cgc aat aag 536
Glu Gly Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Arg Asn Lys
150 155 160

tat gga ctg ctg gcg cgc ttg gca gtg gag gcc ggc ttt gac tgg gtg 584
Tyr Gly Leu Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val
165 170 175

tat tac gag tca aag gcc cac gtg cat tgc tcc gtc aag tcc gag cac 632
Tyr Tyr Glu Ser Lys Ala His Val His Cys Ser Val Lys Ser Glu His
180 185 190

tcg gcc gca gcc aag acg ggc ggc tgc ttc cct gcc gga gcc cag gta 680

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Ser Ala Ala Ala Lys Thr Gly Gly Cys Phe Pro Ala Gly Ala Gln Val
195                 200                 205                 210

cgc ctg gag agt ggg gcg cgt gtg gcc ttg tca gcc gtg agg ccg gga   728
Arg Leu Glu Ser Gly Ala Arg Val Ala Leu Ser Ala Val Arg Pro Gly
                215                 220                 225

gac cgt gtg ctg gcc atg ggg gag gat ggg agc ccc acc ttc agc gat   776
Asp Arg Val Leu Ala Met Gly Glu Asp Gly Ser Pro Thr Phe Ser Asp
            230                 235                 240

gtg ctc att ttc ctg gac cgc gag ccc cac agg ctg aga gcc ttc cag   824
Val Leu Ile Phe Leu Asp Arg Glu Pro His Arg Leu Arg Ala Phe Gln
        245                 250                 255

gtc atc gag act cag gac ccc cca cgc cgc ctg gca ctc aca ccc gct   872
Val Ile Glu Thr Gln Asp Pro Pro Arg Arg Leu Ala Leu Thr Pro Ala
    260                 265                 270

cac ctg ctc ttt acg gct gac aat cac acg gag ccg gca gcc cgc ttc   920
His Leu Leu Phe Thr Ala Asp Asn His Thr Glu Pro Ala Ala Arg Phe
275                 280                 285                 290

cgg gcc aca ttt gcc agc cac gtg cag cct ggc cag tac gtg ctg gtg   968
Arg Ala Thr Phe Ala Ser His Val Gln Pro Gly Gln Tyr Val Leu Val
                295                 300                 305

gct ggg gtg cca ggc ctg cag cct gcc cgc gtg gca gct gtc tct aca   1016
Ala Gly Val Pro Gly Leu Gln Pro Ala Arg Val Ala Ala Val Ser Thr
            310                 315                 320

cac gtg gcc ctc ggg gcc tac gcc ccg ctc aca aag cat ggg aca ctg   1064
His Val Ala Leu Gly Ala Tyr Ala Pro Leu Thr Lys His Gly Thr Leu
        325                 330                 335

gtg gtg gag gat gtg gtg gca tcc tgc ttc gcg gcc gtg gct gac cac   1112
Val Val Glu Asp Val Val Ala Ser Cys Phe Ala Ala Val Ala Asp His
    340                 345                 350

cac ctg gct cag ttg gcc ttc tgg ccc ctg aga ctc ttt cac agc ttg   1160
His Leu Ala Gln Leu Ala Phe Trp Pro Leu Arg Leu Phe His Ser Leu
355                 360                 365                 370

gca tgg ggc agc tgg acc ccg ggg gag ggt gtg cat tgg tac ccc cag   1208
Ala Trp Gly Ser Trp Thr Pro Gly Glu Gly Val His Trp Tyr Pro Gln
                375                 380                 385

ctg ctc tac cgc ctg ggg cgt ctc ctg cta gaa gag ggc agc ttc cac   1256
Leu Leu Tyr Arg Leu Gly Arg Leu Leu Leu Glu Glu Gly Ser Phe His
            390                 395                 400

cca ctg ggc atg tcc ggg gca ggg agc tgaaaggact ccaccgctgc         1303
Pro Leu Gly Met Ser Gly Ala Gly Ser
        405                 410

cctcctggaa ctgctgtact gggtccagaa gcctctcagc caggagggag ctggccctgg 1363
```

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aagggacctg agctggggga cactggctcc tgccatctcc tctgccatga agatacacca 1423

ttgagacttg actgggcaac accagcgtcc cccacccgcg tcgtggtgta gtcatagagc 1483

tgcaagctga gctggcgagg ggatggttgt tgacccctct ctcctagaga ccttgaggct 1543

ggcacggcga ctcccaactc agcctgctct cactacgagt tttcatactc tgcctccccc 1603

attgggaggg cccattccc                                              1622
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<210> 8
<211> 1190
<212> DNA
<213> human Dhh

<220>
<221> CDS
<222> (1)..(1188)

<400> 8

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atg gct ctc ctg acc aat cta ctg ccc ttg tgc tgc ttg gca ctt ctg   48
Met Ala Leu Leu Thr Asn Leu Leu Pro Leu Cys Cys Leu Ala Leu Leu
  1               5                  10                  15

gcg ctg cca gcc cag agc tgc ggg ccg ggc cgg ggg ccg gtt ggc cgg   96
Ala Leu Pro Ala Gln Ser Cys Gly Pro Gly Arg Gly Pro Val Gly Arg
             20                  25                  30

cgc cgc tat gcg cgc aag cag ctc gtg ccg cta ctc tac aag caa ttt   144
Arg Arg Tyr Ala Arg Lys Gln Leu Val Pro Leu Leu Tyr Lys Gln Phe
         35                  40                  45

gtg ccc ggc gtg cca gag cgg acc ctg ggc gcc agt ggg cca gcg gag   192
Val Pro Gly Val Pro Glu Arg Thr Leu Gly Ala Ser Gly Pro Ala Glu
     50                  55                  60

ggg agg gtg gca agg ggc tcc gag cgc ttc cgg gac ctc gtg ccc aac   240
Gly Arg Val Ala Arg Gly Ser Glu Arg Phe Arg Asp Leu Val Pro Asn
 65                  70                  75                  80

tac aac ccc gac atc atc ttc aag gat gag gag aac agt gga gcc gac   288
Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Ser Gly Ala Asp
                 85                  90                  95

cgc ctg atg acc gag cgt tgc aag gag agg gtg aac gct ttg gcc att   336
Arg Leu Met Thr Glu Arg Cys Lys Glu Arg Val Asn Ala Leu Ala Ile
            100                 105                 110

gcc gtg atg aac atg tgg ccc gga gtg cgc cta cga gtg act gag ggc   384
Ala Val Met Asn Met Trp Pro Gly Val Arg Leu Arg Val Thr Glu Gly
        115                 120                 125

tgg gac gag gac ggc cac cac gct cag gat tca ctc cac tac gaa ggc   432
Trp Asp Glu Asp Gly His His Ala Gln Asp Ser Leu His Tyr Glu Gly
    130                 135                 140

cgt gct ttg gac atc act acg tct gac cgc gac cgc aac aag tat ggg   480
```

```
Arg Ala Leu Asp Ile Thr Thr Ser Asp Arg Asp Arg Asn Lys Tyr Gly
145                 150                 155                 160

ttg ctg gcg cgc ctc gca gtg gaa gcc ggc ttc gac tgg gtc tac tac   528
Leu Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val Tyr Tyr
                165                 170                 175

gag tcc cgc aac cac gtc cac gtg tcg gtc aaa gct gat aac tca ctg   576
Glu Ser Arg Asn His Val His Val Ser Val Lys Ala Asp Asn Ser Leu
            180                 185                 190

gcg gtc cgg gcg ggc ggc tgc ttt ccg gga aat gca act gtg cgc ctg   624
Ala Val Arg Ala Gly Gly Cys Phe Pro Gly Asn Ala Thr Val Arg Leu
        195                 200                 205

tgg agc ggc gag cgg aaa ggg ctg cgg gaa ctg cac cgc gga gac tgg   672
Trp Ser Gly Glu Arg Lys Gly Leu Arg Glu Leu His Arg Gly Asp Trp
    210                 215                 220

gtt ttg gcg gcc gat gcg tca ggc cgg gtg gtg ccc acg ccg gtg ctg   720
Val Leu Ala Ala Asp Ala Ser Gly Arg Val Val Pro Thr Pro Val Leu
225                 230                 235                 240

ctc ttc ctg gac cgg gac ttg cag cgc cgg gct tca ttt gtg gct gtg   768
Leu Phe Leu Asp Arg Asp Leu Gln Arg Arg Ala Ser Phe Val Ala Val
                245                 250                 255

gag acc gag tgg cct cca cgc aaa ctg ttg ctc acg ccc tgg cac ctg   816
Glu Thr Glu Trp Pro Pro Arg Lys Leu Leu Leu Thr Pro Trp His Leu
            260                 265                 270

gtg ttt gcc gct cga ggg ccg gcg ccc gcg cca ggc gac ttt gca ccg   864
Val Phe Ala Ala Arg Gly Pro Ala Pro Ala Pro Gly Asp Phe Ala Pro
        275                 280                 285

gtg ttc gcg cgc cgg cta cgc gct ggg gac tcg gtg ctg gcg ccc ggc   912
Val Phe Ala Arg Arg Leu Arg Ala Gly Asp Ser Val Leu Ala Pro Gly
    290                 295                 300

ggg gat gcg ctt cgg cca gcg cgc gtg gcc cgt gtg gcg cgg gag gaa   960
Gly Asp Ala Leu Arg Pro Ala Arg Val Ala Arg Val Ala Arg Glu Glu
305                 310                 315                 320

gcc gtg ggc gtg ttc gcg ccg ctc acc gcg cac ggg acg ctg ctg gtg   1008
Ala Val Gly Val Phe Ala Pro Leu Thr Ala His Gly Thr Leu Leu Val
                325                 330                 335

aac gat gtc ctg gcc tct tgc tac gcg gtt ctg gag agt cac cag tgg   1056
Asn Asp Val Leu Ala Ser Cys Tyr Ala Val Leu Glu Ser His Gln Trp
            340                 345                 350

gcg cac cgc gct ttt gcc ccc ttg aga ctg ctg cac gcg cta ggg gcg   1104
Ala His Arg Ala Phe Ala Pro Leu Arg Leu Leu His Ala Leu Gly Ala
        355                 360                 365

ctg ctc ccc ggc ggg gcc gtc cag ccg act ggc atg cat tgg tac tct   1152
Leu Leu Pro Gly Gly Ala Val Gln Pro Thr Gly Met His Trp Tyr Ser
```

```
    370                 375                 380

cgg ctc ctc tac cgc tta gcg gag gag cta ctg ggc tg                1190
Arg Leu Leu Tyr Arg Leu Ala Glu Glu Leu Leu Gly
385                 390                 395

<210> 9
<211> 1251
<212> DNA
<213> Zebrafish Thh

<220>
<221> CDS
<222> (1)..(1248)

<400> 9
atg gac gta agg ctg cat ctg aag caa ttt gct tta ctg tgt ttt atc    48
Met Asp Val Arg Leu His Leu Lys Gln Phe Ala Leu Leu Cys Phe Ile
  1               5                  10                  15

agc ttg ctt ctg acg cct tgt gga tta gcc tgt ggt cct ggt aga ggt    96
Ser Leu Leu Leu Thr Pro Cys Gly Leu Ala Cys Gly Pro Gly Arg Gly
             20                  25                  30

tat gga aaa cga aga cac cca aag aaa tta acc ccg ttg gct tac aag   144
Tyr Gly Lys Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys
         35                  40                  45

caa ttc atc ccc aac gtt gct gag aaa acg ctt gga gcc agc ggc aaa   192
Gln Phe Ile Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Lys
     50                  55                  60

tac gaa ggc aaa atc aca agg aat tca gag aga ttt aaa gag ctg att   240
Tyr Glu Gly Lys Ile Thr Arg Asn Ser Glu Arg Phe Lys Glu Leu Ile
 65                  70                  75                  80

ccg aat tat aat ccc gat atc atc ttt aag gac gag gaa aac aca aac   288
Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Asn
                 85                  90                  95

gct gac agg ctg atg acc aag cgc tgt aag gac aag tta aat tcg ttg   336
Ala Asp Arg Leu Met Thr Lys Arg Cys Lys Asp Lys Leu Asn Ser Leu
            100                 105                 110

gcc ata tcc gtc atg aac cac tgg ccc ggc gtg aaa ctg cgc gtc act   384
Ala Ile Ser Val Met Asn His Trp Pro Gly Val Lys Leu Arg Val Thr
        115                 120                 125

gaa ggc tgg gat gag gat ggt cac cat tta gaa gaa tct ttg cac tat   432
Glu Gly Trp Asp Glu Asp Gly His His Leu Glu Glu Ser Leu His Tyr
    130                 135                 140

gag gga cgg gca gtg gac atc act acc tca gac agg gat aaa agc aag   480
Glu Gly Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Lys Ser Lys
145                 150                 155                 160

tat ggg atg cta tcc agg ctt gca gtg gag gca gga ttc gac tgg gtc   528
```

```
Tyr Gly Met Leu Ser Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val
                165                 170                 175

tat tat gaa tct aaa gcc cac ata cac tgc tct gtc aaa gca gaa aat   576
Tyr Tyr Glu Ser Lys Ala His Ile His Cys Ser Val Lys Ala Glu Asn
            180                 185                 190

tca gtg gct gct aaa tca gga gga tgt ttt cct ggg tct ggg acg gtg   624
Ser Val Ala Ala Lys Ser Gly Gly Cys Phe Pro Gly Ser Gly Thr Val
        195                 200                 205

aca ctt ggt gat ggg acg agg aaa ccc atc aaa gat ctt aaa gtg ggc   672
Thr Leu Gly Asp Gly Thr Arg Lys Pro Ile Lys Asp Leu Lys Val Gly
    210                 215                 220

gac cgg gtt ttg gct gca gac gag aag gga aat gtc tta ata agc gac   720
Asp Arg Val Leu Ala Ala Asp Glu Lys Gly Asn Val Leu Ile Ser Asp
225                 230                 235                 240

ttt att atg ttt ata gac cac gat ccg aca acg aga agg caa ttc atc   768
Phe Ile Met Phe Ile Asp His Asp Pro Thr Thr Arg Arg Gln Phe Ile
                245                 250                 255

gtc atc gag acg tca gaa cct ttc acc aag ctc acc ctc act gcc gcg   816
Val Ile Glu Thr Ser Glu Pro Phe Thr Lys Leu Thr Leu Thr Ala Ala
            260                 265                 270

cac cta gtt ttc gtt gga aac tct tca gca gct tcg ggt ata aca gca   864
His Leu Val Phe Val Gly Asn Ser Ser Ala Ala Ser Gly Ile Thr Ala
        275                 280                 285

aca ttt gcc agc aac gtg aag cct gga gat aca gtt tta gtg tgg gaa   912
Thr Phe Ala Ser Asn Val Lys Pro Gly Asp Thr Val Leu Val Trp Glu
    290                 295                 300

gac aca tgc gag agc ctc aag agc gtt aca gtg aaa agg att tac act   960
Asp Thr Cys Glu Ser Leu Lys Ser Val Thr Val Lys Arg Ile Tyr Thr
305                 310                 315                 320

gag gag cac gag ggc tct ttt gcg cca gtc acc gcg cac gga acc ata  1008
Glu Glu His Glu Gly Ser Phe Ala Pro Val Thr Ala His Gly Thr Ile
                325                 330                 335

ata gtg gat cag gtg ttg gca tcg tgc tac gcg gtc att gag aac cac  1056
Ile Val Asp Gln Val Leu Ala Ser Cys Tyr Ala Val Ile Glu Asn His
            340                 345                 350

aaa tgg gca cat tgg gct ttt gcg ccg gtc agg ttg tgt cac aag ctg  1104
Lys Trp Ala His Trp Ala Phe Ala Pro Val Arg Leu Cys His Lys Leu
        355                 360                 365

atg acg tgg ctt ttt ccg gct cgt gaa tca aac gtc aat ttt cag gag  1152
Met Thr Trp Leu Phe Pro Ala Arg Glu Ser Asn Val Asn Phe Gln Glu
    370                 375                 380

gat ggt atc cac tgg tac tca aat atg ctg ttt cac atc ggc tct tgg  1200
Asp Gly Ile His Trp Tyr Ser Asn Met Leu Phe His Ile Gly Ser Trp
```

```
385                 390                 395                 400

ctg ctg gac aga gac tct ttc cat cca ctc ggg att tta cac tta agt   1248
Leu Leu Asp Arg Asp Ser Phe His Pro Leu Gly Ile Leu His Leu Ser
                405                 410                 415

tga                                                               1251
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<210> 10
<211> 425
<212> PRT
<213> chicken Shh

<400> 10

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Met Val Glu Met Leu Leu Leu Thr Arg Ile Leu Leu Val Gly Phe Ile
  1               5                  10                  15

Cys Ala Leu Leu Val Ser Ser Gly Leu Thr Cys Gly Pro Gly Arg Gly
             20                  25                  30

Ile Gly Lys Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys
         35                  40                  45

Gln Phe Ile Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Arg
     50                  55                  60

Tyr Glu Gly Lys Ile Thr Arg Asn Ser Glu Arg Phe Lys Glu Leu Thr
 65                  70                  75                  80

Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Gly
                 85                  90                  95

Ala Asp Arg Leu Met Thr Gln Arg Cys Lys Asp Lys Leu Asn Ala Leu
            100                 105                 110

Ala Ile Ser Val Met Asn Gln Trp Pro Gly Val Lys Leu Arg Val Thr
        115                 120                 125

Glu Gly Trp Asp Glu Asp Gly His His Ser Glu Glu Ser Leu His Tyr
    130                 135                 140

Glu Gly Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Arg Ser Lys
145                 150                 155                 160

Tyr Gly Met Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val
                165                 170                 175

Tyr Tyr Glu Ser Lys Ala His Ile His Cys Ser Val Lys Ala Glu Asn
            180                 185                 190

Ser Val Ala Ala Lys Ser Gly Gly Cys Phe Pro Gly Ser Ala Thr Val
        195                 200                 205

His Leu Glu His Gly Gly Thr Lys Leu Val Lys Asp Leu Ser Pro Gly
    210                 215                 220

Asp Arg Val Leu Ala Ala Asp Ala Asp Gly Arg Leu Leu Tyr Ser Asp
```

225 230 235 240

Phe Leu Thr Phe Leu Asp Arg Met Asp Ser Ser Arg Lys Leu Phe Tyr
245 250 255

Val Ile Glu Thr Arg Gln Pro Arg Ala Arg Leu Leu Leu Thr Ala Ala
260 265 270

His Leu Leu Phe Val Ala Pro Gln His Asn Gln Ser Glu Ala Thr Gly
275 280 285

Ser Thr Ser Gly Gln Ala Leu Phe Ala Ser Asn Val Lys Pro Gly Gln
290 295 300

Arg Val Tyr Val Leu Gly Glu Gly Gly Gln Gln Leu Leu Pro Ala Ser
305 310 315 320

Val His Ser Val Ser Leu Arg Glu Glu Ala Ser Gly Ala Tyr Ala Pro
325 330 335

Leu Thr Ala Gln Gly Thr Ile Leu Ile Asn Arg Val Leu Ala Ser Cys
340 345 350

Tyr Ala Val Ile Glu Glu His Ser Trp Ala His Trp Ala Phe Ala Pro
355 360 365

Phe Arg Leu Ala Gln Gly Leu Leu Ala Ala Leu Cys Pro Asp Gly Ala
370 375 380

Ile Pro Thr Ala Ala Thr Thr Thr Thr Gly Ile His Trp Tyr Ser Arg
385 390 395 400

Leu Leu Tyr Arg Ile Gly Ser Trp Val Leu Asp Gly Asp Ala Leu His
405 410 415

Pro Leu Gly Met Val Ala Pro Ala Ser
420 425

<210> 11
<211> 396
<212> PRT
<213> mouse Dhh

<400> 11
Met Ala Leu Pro Ala Ser Leu Leu Pro Leu Cys Cys Leu Ala Leu Leu
1 5 10 15

Ala Leu Ser Ala Gln Ser Cys Gly Pro Gly Arg Gly Pro Val Gly Arg
20 25 30

Arg Arg Tyr Val Arg Lys Gln Leu Val Pro Leu Leu Tyr Lys Gln Phe
35 40 45

Val Pro Ser Met Pro Glu Arg Thr Leu Gly Ala Ser Gly Pro Ala Glu
50 55 60

Gly Arg Val Thr Arg Gly Ser Glu Arg Phe Arg Asp Leu Val Pro Asn

```
 65                  70                  75                  80

Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Ser Gly Ala Asp
                 85                  90                  95

Arg Leu Met Thr Glu Arg Cys Lys Glu Arg Val Asn Ala Leu Ala Ile
            100                 105                 110

Ala Val Met Asn Met Trp Pro Gly Val Arg Leu Arg Val Thr Glu Gly
        115                 120                 125

Trp Asp Glu Asp Gly His His Ala Gln Asp Ser Leu His Tyr Glu Gly
    130                 135                 140

Arg Ala Leu Asp Ile Thr Thr Ser Asp Arg Asp Arg Asn Lys Tyr Gly
145                 150                 155                 160

Leu Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val Tyr Tyr
                165                 170                 175

Glu Ser Arg Asn His Ile His Val Ser Val Lys Ala Asp Asn Ser Leu
            180                 185                 190

Ala Val Arg Ala Gly Gly Cys Phe Pro Gly Asn Ala Thr Val Arg Leu
        195                 200                 205

Arg Ser Gly Glu Arg Lys Gly Leu Arg Glu Leu His Arg Gly Asp Trp
    210                 215                 220

Val Leu Ala Ala Asp Ala Ala Gly Arg Val Val Pro Thr Pro Val Leu
225                 230                 235                 240

Leu Phe Leu Asp Arg Asp Leu Gln Arg Arg Ala Ser Phe Val Ala Val
                245                 250                 255

Glu Thr Glu Arg Pro Pro Arg Lys Leu Leu Leu Thr Pro Trp His Leu
            260                 265                 270

Val Phe Ala Ala Arg Gly Pro Ala Pro Ala Pro Gly Asp Phe Ala Pro
        275                 280                 285

Val Phe Ala Arg Arg Leu Arg Ala Gly Asp Ser Val Leu Ala Pro Gly
    290                 295                 300

Gly Asp Ala Leu Gln Pro Ala Arg Val Ala Arg Val Ala Arg Glu Glu
305                 310                 315                 320

Ala Val Gly Val Phe Ala Pro Leu Thr Ala His Gly Thr Leu Leu Val
                325                 330                 335

Asn Asp Val Leu Ala Ser Cys Tyr Ala Val Leu Glu Ser His Gln Trp
            340                 345                 350

Ala His Arg Ala Phe Ala Pro Leu Arg Leu Leu His Ala Leu Gly Ala
        355                 360                 365

Leu Leu Pro Gly Gly Ala Val Gln Pro Thr Gly Met His Trp Tyr Ser
```

```
    370                 375                 380

Arg Leu Leu Tyr Arg Leu Ala Glu Glu Leu Met Gly
385                 390                 395

<210> 12
<211> 411
<212> PRT
<213> mouse Ihh

<400> 12
Met Ser Pro Ala Trp Leu Arg Pro Arg Leu Arg Phe Cys Leu Phe Leu
  1               5                  10                  15

Leu Leu Leu Leu Leu Val Pro Ala Ala Arg Gly Cys Gly Pro Gly Arg
             20                  25                  30

Val Val Gly Ser Arg Arg Arg Pro Pro Arg Lys Leu Val Pro Leu Ala
         35                  40                  45

Tyr Lys Gln Phe Ser Pro Asn Val Pro Glu Lys Thr Leu Gly Ala Ser
     50                  55                  60

Gly Arg Tyr Glu Gly Lys Ile Ala Arg Ser Ser Glu Arg Phe Lys Glu
 65                  70                  75                  80

Leu Thr Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn
                 85                  90                  95

Thr Gly Ala Asp Arg Leu Met Thr Gln Arg Cys Lys Asp Arg Leu Asn
            100                 105                 110

Ser Leu Ala Ile Ser Val Met Asn Gln Trp Pro Gly Val Lys Leu Arg
        115                 120                 125

Val Thr Glu Gly Arg Asp Glu Asp Gly His His Ser Glu Glu Ser Leu
    130                 135                 140

His Tyr Glu Gly Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Arg
145                 150                 155                 160

Asn Lys Tyr Gly Leu Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp
                165                 170                 175

Trp Val Tyr Tyr Glu Ser Lys Ala His Val His Cys Ser Val Lys Ser
            180                 185                 190

Glu His Ser Ala Ala Ala Lys Thr Gly Gly Cys Phe Pro Ala Gly Ala
        195                 200                 205

Gln Val Arg Leu Glu Asn Gly Glu Arg Val Ala Leu Ser Ala Val Lys
    210                 215                 220

Pro Gly Asp Arg Val Leu Ala Met Gly Glu Asp Gly Thr Pro Thr Phe
225                 230                 235                 240

Ser Asp Val Leu Ile Phe Leu Asp Arg Glu Pro Asn Arg Leu Arg Ala
```

```
                245                 250                 255

Phe Gln Val Ile Glu Thr Gln Asp Pro Pro Arg Arg Leu Ala Leu Thr
            260                 265                 270

Pro Ala His Leu Leu Phe Ile Ala Asp Asn His Thr Glu Pro Ala Ala
        275                 280                 285

His Phe Arg Ala Thr Phe Ala Ser His Val Gln Pro Gly Gln Tyr Val
    290                 295                 300

Leu Val Ser Gly Val Pro Gly Leu Gln Pro Ala Arg Val Ala Ala Val
305                 310                 315                 320

Ser Thr His Val Ala Leu Gly Ser Tyr Ala Pro Leu Thr Arg His Gly
                325                 330                 335

Thr Leu Val Val Glu Asp Val Val Ala Ser Cys Phe Ala Ala Val Ala
            340                 345                 350

Asp His His Leu Ala Gln Leu Ala Phe Trp Pro Leu Arg Leu Phe Pro
        355                 360                 365

Ser Leu Ala Trp Gly Ser Trp Thr Pro Ser Glu Gly Val His Ser Tyr
    370                 375                 380

Pro Gln Met Leu Tyr Arg Leu Gly Arg Leu Leu Leu Glu Glu Ser Thr
385                 390                 395                 400

Phe His Pro Leu Gly Met Ser Gly Ala Gly Ser
                405                 410

<210> 13
<211> 437
<212> PRT
<213> mouse Shh

<400> 13
Met Leu Leu Leu Leu Ala Arg Cys Phe Leu Val Ile Leu Ala Ser Ser
  1               5                  10                  15

Leu Leu Val Cys Pro Gly Leu Ala Cys Gly Pro Gly Arg Gly Phe Gly
             20                  25                  30

Lys Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys Gln Phe
         35                  40                  45

Ile Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Arg Tyr Glu
     50                  55                  60

Gly Lys Ile Thr Arg Asn Ser Glu Arg Phe Lys Glu Leu Thr Pro Asn
 65                  70                  75                  80

Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Gly Ala Asp
                 85                  90                  95

Arg Leu Met Thr Gln Arg Cys Lys Asp Lys Leu Asn Ala Leu Ala Ile
```

```
            100                 105                 110

Ser Val Met Asn Gln Trp Pro Gly Val Arg Leu Arg Val Thr Glu Gly
        115                 120                 125

Trp Asp Glu Asp Gly His His Ser Glu Glu Ser Leu His Tyr Glu Gly
    130                 135                 140

Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Arg Ser Lys Tyr Gly
145                 150                 155                 160

Met Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val Tyr Tyr
                165                 170                 175

Glu Ser Lys Ala His Ile His Cys Ser Val Lys Ala Glu Asn Ser Val
            180                 185                 190

Ala Ala Lys Ser Gly Gly Cys Phe Pro Gly Ser Ala Thr Val His Leu
        195                 200                 205

Glu Gln Gly Gly Thr Lys Leu Val Lys Asp Leu Arg Pro Gly Asp Arg
    210                 215                 220

Val Leu Ala Ala Asp Asp Gln Gly Arg Leu Leu Tyr Ser Asp Phe Leu
225                 230                 235                 240

Thr Phe Leu Asp Arg Asp Glu Gly Ala Lys Lys Val Phe Tyr Val Ile
                245                 250                 255

Glu Thr Leu Glu Pro Arg Glu Arg Leu Leu Leu Thr Ala Ala His Leu
            260                 265                 270

Leu Phe Val Ala Pro His Asn Asp Ser Gly Pro Thr Pro Gly Pro Ser
        275                 280                 285

Ala Leu Phe Ala Ser Arg Val Arg Pro Gly Gln Arg Val Tyr Val Val
    290                 295                 300

Ala Glu Arg Gly Gly Asp Arg Arg Leu Leu Pro Ala Ala Val His Ser
305                 310                 315                 320

Val Thr Leu Arg Glu Glu Glu Ala Gly Ala Tyr Ala Pro Leu Thr Ala
                325                 330                 335

His Gly Thr Ile Leu Ile Asn Arg Val Leu Ala Ser Cys Tyr Ala Val
            340                 345                 350

Ile Glu Glu His Ser Trp Ala His Arg Ala Phe Ala Pro Phe Arg Leu
        355                 360                 365

Ala His Ala Leu Leu Ala Ala Leu Ala Pro Ala Arg Thr Asp Gly Gly
    370                 375                 380

Gly Gly Gly Ser Ile Pro Ala Ala Gln Ser Ala Thr Glu Ala Arg Gly
385                 390                 395                 400

Ala Glu Pro Thr Ala Gly Ile His Trp Tyr Ser Gln Leu Leu Tyr His
```

```
                405                 410                 415

Ile Gly Thr Trp Leu Leu Asp Ser Glu Thr Met His Pro Leu Gly Met
            420                 425                 430

Ala Val Lys Ser Ser
        435
```

<210> 14
<211> 418
<212> PRT
<213> zebrafish Shh

<400> 14

```
Met Arg Leu Leu Thr Arg Val Leu Leu Val Ser Leu Leu Thr Leu Ser
  1               5                  10                  15

Leu Val Val Ser Gly Leu Ala Cys Gly Pro Gly Arg Gly Tyr Gly Arg
             20                  25                  30

Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys Gln Phe Ile
         35                  40                  45

Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Arg Tyr Glu Gly
     50                  55                  60

Lys Ile Thr Arg Asn Ser Glu Arg Phe Lys Glu Leu Thr Pro Asn Tyr
 65                  70                  75                  80

Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Gly Ala Asp Arg
                 85                  90                  95

Leu Met Thr Gln Arg Cys Lys Asp Lys Leu Asn Ser Leu Ala Ile Ser
            100                 105                 110

Val Met Asn His Trp Pro Gly Val Lys Leu Arg Val Thr Glu Gly Trp
        115                 120                 125

Asp Glu Asp Gly His His Phe Glu Glu Ser Leu His Tyr Glu Gly Arg
    130                 135                 140

Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Lys Ser Lys Tyr Gly Thr
145                 150                 155                 160

Leu Ser Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val Tyr Tyr Glu
                165                 170                 175

Ser Lys Ala His Ile His Cys Ser Val Lys Ala Glu Asn Ser Val Ala
            180                 185                 190

Ala Lys Ser Gly Gly Cys Phe Pro Gly Ser Ala Leu Val Ser Leu Gln
        195                 200                 205

Asp Gly Gly Gln Lys Ala Val Lys Asp Leu Asn Pro Gly Asp Lys Val
    210                 215                 220

Leu Ala Ala Asp Ser Ala Gly Asn Leu Val Phe Ser Asp Phe Ile Met
```

225 230 235 240

Phe Thr Asp Arg Asp Ser Thr Thr Arg Arg Val Phe Tyr Val Ile Glu
245 250 255

Thr Gln Glu Pro Val Glu Lys Ile Thr Leu Thr Ala Ala His Leu Leu
260 265 270

Phe Val Leu Asp Asn Ser Thr Glu Asp Leu His Thr Met Thr Ala Ala
275 280 285

Tyr Ala Ser Ser Val Arg Ala Gly Gln Lys Val Met Val Val Asp Asp
290 295 300

Ser Gly Gln Leu Lys Ser Val Ile Val Gln Arg Ile Tyr Thr Glu Glu
305 310 315 320

Gln Arg Gly Ser Phe Ala Pro Val Thr Ala His Gly Thr Ile Val Val
325 330 335

Asp Arg Ile Leu Ala Ser Cys Tyr Ala Val Ile Glu Asp Gln Gly Leu
340 345 350

Ala His Leu Ala Phe Ala Pro Ala Arg Leu Tyr Tyr Tyr Val Ser Ser
355 360 365

Phe Leu Ser Pro Lys Thr Pro Ala Val Gly Pro Met Arg Leu Tyr Asn
370 375 380

Arg Arg Gly Ser Thr Gly Thr Pro Gly Ser Cys His Gln Met Gly Thr
385 390 395 400

Trp Leu Leu Asp Ser Asn Met Leu His Pro Leu Gly Met Ser Val Asn
405 410 415

Ser Ser

<210> 15
<211> 475
<212> PRT
<213> human Shh

<220>
<223> Xaa at position 463 is any or unknown amino acid

<400> 15
Met Leu Leu Leu Ala Arg Cys Leu Leu Leu Val Leu Val Ser Ser Leu
1 5 10 15

Leu Val Cys Ser Gly Leu Ala Cys Gly Pro Gly Arg Gly Phe Gly Lys
20 25 30

Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys Gln Phe Ile
35 40 45

Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Arg Tyr Glu Gly
50 55 60

```
Lys Ile Ser Arg Asn Ser Glu Arg Phe Lys Glu Leu Thr Pro Asn Tyr
 65                  70                  75                  80

Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Gly Ala Asp Arg
                 85                  90                  95

Leu Met Thr Gln Arg Cys Lys Asp Lys Leu Asn Ala Leu Ala Ile Ser
            100                 105                 110

Val Met Asn Gln Trp Pro Gly Val Lys Leu Arg Val Thr Glu Gly Trp
        115                 120                 125

Asp Glu Asp Gly His His Ser Glu Glu Ser Leu His Tyr Glu Gly Arg
    130                 135                 140

Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Arg Ser Lys Tyr Gly Met
145                 150                 155                 160

Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val Tyr Tyr Glu
                165                 170                 175

Ser Lys Ala His Ile His Cys Ser Val Lys Ala Glu Asn Ser Val Ala
            180                 185                 190

Ala Lys Ser Gly Gly Cys Phe Pro Gly Ser Ala Thr Val His Leu Glu
        195                 200                 205

Gln Gly Gly Thr Lys Leu Val Lys Asp Leu Ser Pro Gly Asp Arg Val
    210                 215                 220

Leu Ala Ala Asp Asp Gln Gly Arg Leu Leu Tyr Ser Asp Phe Leu Thr
225                 230                 235                 240

Phe Leu Asp Arg Asp Asp Gly Ala Lys Lys Val Phe Tyr Val Ile Glu
                245                 250                 255

Thr Arg Glu Pro Arg Glu Arg Leu Leu Leu Thr Ala Ala His Leu Leu
            260                 265                 270

Phe Val Ala Pro His Asn Asp Ser Ala Thr Gly Glu Pro Glu Ala Ser
        275                 280                 285

Ser Gly Ser Gly Pro Pro Ser Gly Gly Ala Leu Gly Pro Arg Ala Leu
    290                 295                 300

Phe Ala Ser Arg Val Arg Pro Gly Gln Arg Val Tyr Val Val Ala Glu
305                 310                 315                 320

Arg Asp Gly Asp Arg Arg Leu Leu Pro Ala Ala Val His Ser Val Thr
                325                 330                 335

Leu Ser Glu Glu Ala Ala Gly Ala Tyr Ala Pro Leu Thr Ala Gln Gly
            340                 345                 350

Thr Ile Leu Ile Asn Arg Val Leu Ala Ser Cys Tyr Ala Val Ile Glu
        355                 360                 365
```

```
Glu His Ser Trp Ala His Arg Ala Phe Ala Pro Phe Arg Leu Ala His
    370                 375                 380

Ala Leu Leu Ala Ala Leu Ala Pro Ala Arg Thr Asp Arg Gly Gly Asp
385                 390                 395                 400

Ser Gly Gly Gly Asp Arg Gly Gly Gly Gly Gly Arg Val Ala Leu Thr
                405                 410                 415

Ala Pro Gly Ala Ala Asp Ala Pro Gly Ala Gly Ala Thr Ala Gly Ile
            420                 425                 430

His Trp Tyr Ser Gln Leu Leu Tyr Gln Ile Gly Thr Trp Leu Leu Asp
        435                 440                 445

Ser Glu Ala Leu His Pro Leu Gly Met Ala Val Lys Ser Ser Xaa Ser
    450                 455                 460

Arg Gly Ala Gly Gly Gly Ala Arg Glu Gly Ala
465                 470                 475
```

<210> 16
<211> 411
<212> PRT
<213> human Ihh

<400> 16

```
Met Ser Pro Ala Arg Leu Arg Pro Arg Leu His Phe Cys Leu Val Leu
  1               5                  10                  15

Leu Leu Leu Leu Val Val Pro Ala Ala Trp Gly Cys Gly Pro Gly Arg
             20                  25                  30

Val Val Gly Ser Arg Arg Arg Pro Pro Arg Lys Leu Val Pro Leu Ala
         35                  40                  45

Tyr Lys Gln Phe Ser Pro Asn Val Pro Glu Lys Thr Leu Gly Ala Ser
     50                  55                  60

Gly Arg Tyr Glu Gly Lys Ile Ala Arg Ser Ser Glu Arg Phe Lys Glu
 65                  70                  75                  80

Leu Thr Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn
                 85                  90                  95

Thr Gly Ala Asp Arg Leu Met Thr Gln Arg Cys Lys Asp Arg Leu Asn
            100                 105                 110

Ser Leu Ala Ile Ser Val Met Asn Gln Trp Pro Gly Val Lys Leu Arg
        115                 120                 125

Val Thr Glu Gly Trp Asp Glu Asp Gly His His Ser Glu Glu Ser Leu
    130                 135                 140

His Tyr Glu Gly Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Arg
145                 150                 155                 160
```

```
Asn Lys Tyr Gly Leu Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp
                165                 170                 175

Trp Val Tyr Tyr Glu Ser Lys Ala His Val His Cys Ser Val Lys Ser
            180                 185                 190

Glu His Ser Ala Ala Ala Lys Thr Gly Gly Cys Phe Pro Ala Gly Ala
        195                 200                 205

Gln Val Arg Leu Glu Ser Gly Ala Arg Val Ala Leu Ser Ala Val Arg
    210                 215                 220

Pro Gly Asp Arg Val Leu Ala Met Gly Glu Asp Gly Ser Pro Thr Phe
225                 230                 235                 240

Ser Asp Val Leu Ile Phe Leu Asp Arg Glu Pro His Arg Leu Arg Ala
                245                 250                 255

Phe Gln Val Ile Glu Thr Gln Asp Pro Pro Arg Arg Leu Ala Leu Thr
            260                 265                 270

Pro Ala His Leu Leu Phe Thr Ala Asp Asn His Thr Glu Pro Ala Ala
        275                 280                 285

Arg Phe Arg Ala Thr Phe Ala Ser His Val Gln Pro Gly Gln Tyr Val
    290                 295                 300

Leu Val Ala Gly Val Pro Gly Leu Gln Pro Ala Arg Val Ala Ala Val
305                 310                 315                 320

Ser Thr His Val Ala Leu Gly Ala Tyr Ala Pro Leu Thr Lys His Gly
                325                 330                 335

Thr Leu Val Val Glu Asp Val Val Ala Ser Cys Phe Ala Ala Val Ala
            340                 345                 350

Asp His His Leu Ala Gln Leu Ala Phe Trp Pro Leu Arg Leu Phe His
        355                 360                 365

Ser Leu Ala Trp Gly Ser Trp Thr Pro Gly Glu Gly Val His Trp Tyr
    370                 375                 380

Pro Gln Leu Leu Tyr Arg Leu Gly Arg Leu Leu Leu Glu Glu Gly Ser
385                 390                 395                 400

Phe His Pro Leu Gly Met Ser Gly Ala Gly Ser
                405                 410
```

<210> 17
<211> 396
<212> PRT
<213> human Dhh

<400> 17

```
Met Ala Leu Leu Thr Asn Leu Leu Pro Leu Cys Cys Leu Ala Leu Leu
  1               5                  10                  15
```

```
Ala Leu Pro Ala Gln Ser Cys Gly Pro Gly Arg Gly Pro Val Gly Arg
            20                  25                  30

Arg Arg Tyr Ala Arg Lys Gln Leu Val Pro Leu Leu Tyr Lys Gln Phe
        35                  40                  45

Val Pro Gly Val Pro Glu Arg Thr Leu Gly Ala Ser Gly Pro Ala Glu
    50                  55                  60

Gly Arg Val Ala Arg Gly Ser Glu Arg Phe Arg Asp Leu Val Pro Asn
65                  70                  75                  80

Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Ser Gly Ala Asp
                85                  90                  95

Arg Leu Met Thr Glu Arg Cys Lys Glu Arg Val Asn Ala Leu Ala Ile
            100                 105                 110

Ala Val Met Asn Met Trp Pro Gly Val Arg Leu Arg Val Thr Glu Gly
        115                 120                 125

Trp Asp Glu Asp Gly His His Ala Gln Asp Ser Leu His Tyr Glu Gly
    130                 135                 140

Arg Ala Leu Asp Ile Thr Thr Ser Asp Arg Asp Arg Asn Lys Tyr Gly
145                 150                 155                 160

Leu Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val Tyr Tyr
                165                 170                 175

Glu Ser Arg Asn His Val His Val Ser Val Lys Ala Asp Asn Ser Leu
            180                 185                 190

Ala Val Arg Ala Gly Gly Cys Phe Pro Gly Asn Ala Thr Val Arg Leu
        195                 200                 205

Trp Ser Gly Glu Arg Lys Gly Leu Arg Glu Leu His Arg Gly Asp Trp
    210                 215                 220

Val Leu Ala Ala Asp Ala Ser Gly Arg Val Val Pro Thr Pro Val Leu
225                 230                 235                 240

Leu Phe Leu Asp Arg Asp Leu Gln Arg Arg Ala Ser Phe Val Ala Val
                245                 250                 255

Glu Thr Glu Trp Pro Pro Arg Lys Leu Leu Leu Thr Pro Trp His Leu
            260                 265                 270

Val Phe Ala Ala Arg Gly Pro Ala Pro Ala Pro Gly Asp Phe Ala Pro
        275                 280                 285

Val Phe Ala Arg Arg Leu Arg Ala Gly Asp Ser Val Leu Ala Pro Gly
    290                 295                 300

Gly Asp Ala Leu Arg Pro Ala Arg Val Ala Arg Val Ala Arg Glu Glu
305                 310                 315                 320
```

```
Ala Val Gly Val Phe Ala Pro Leu Thr Ala His Gly Thr Leu Leu Val
                325                 330                 335

Asn Asp Val Leu Ala Ser Cys Tyr Ala Val Leu Glu Ser His Gln Trp
            340                 345                 350

Ala His Arg Ala Phe Ala Pro Leu Arg Leu Leu His Ala Leu Gly Ala
        355                 360                 365

Leu Leu Pro Gly Gly Ala Val Gln Pro Thr Gly Met His Trp Tyr Ser
    370                 375                 380

Arg Leu Leu Tyr Arg Leu Ala Glu Glu Leu Leu Gly
385                 390                 395
```

<210> 18
<211> 416
<212> PRT
<213> Zebrafish Thh

<400> 18

```
Met Asp Val Arg Leu His Leu Lys Gln Phe Ala Leu Leu Cys Phe Ile
  1               5                  10                  15

Ser Leu Leu Leu Thr Pro Cys Gly Leu Ala Cys Gly Pro Gly Arg Gly
             20                  25                  30

Tyr Gly Lys Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys
         35                  40                  45

Gln Phe Ile Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Lys
     50                  55                  60

Tyr Glu Gly Lys Ile Thr Arg Asn Ser Glu Arg Phe Lys Glu Leu Ile
 65                  70                  75                  80

Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Asn
                 85                  90                  95

Ala Asp Arg Leu Met Thr Lys Arg Cys Lys Asp Lys Leu Asn Ser Leu
            100                 105                 110

Ala Ile Ser Val Met Asn His Trp Pro Gly Val Lys Leu Arg Val Thr
        115                 120                 125

Glu Gly Trp Asp Glu Asp Gly His His Leu Glu Glu Ser Leu His Tyr
    130                 135                 140

Glu Gly Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Lys Ser Lys
145                 150                 155                 160

Tyr Gly Met Leu Ser Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val
                165                 170                 175

Tyr Tyr Glu Ser Lys Ala His Ile His Cys Ser Val Lys Ala Glu Asn
            180                 185                 190
```

```
Ser Val Ala Ala Lys Ser Gly Gly Cys Phe Pro Gly Ser Gly Thr Val
        195                 200                 205

Thr Leu Gly Asp Gly Thr Arg Lys Pro Ile Lys Asp Leu Lys Val Gly
    210                 215                 220

Asp Arg Val Leu Ala Ala Asp Glu Lys Gly Asn Val Leu Ile Ser Asp
225                 230                 235                 240

Phe Ile Met Phe Ile Asp His Asp Pro Thr Thr Arg Arg Gln Phe Ile
                245                 250                 255

Val Ile Glu Thr Ser Glu Pro Phe Thr Lys Leu Thr Leu Thr Ala Ala
            260                 265                 270

His Leu Val Phe Val Gly Asn Ser Ser Ala Ala Ser Gly Ile Thr Ala
        275                 280                 285

Thr Phe Ala Ser Asn Val Lys Pro Gly Asp Thr Val Leu Val Trp Glu
    290                 295                 300

Asp Thr Cys Glu Ser Leu Lys Ser Val Thr Val Lys Arg Ile Tyr Thr
305                 310                 315                 320

Glu Glu His Glu Gly Ser Phe Ala Pro Val Thr Ala His Gly Thr Ile
                325                 330                 335

Ile Val Asp Gln Val Leu Ala Ser Cys Tyr Ala Val Ile Glu Asn His
            340                 345                 350

Lys Trp Ala His Trp Ala Phe Ala Pro Val Arg Leu Cys His Lys Leu
        355                 360                 365

Met Thr Trp Leu Phe Pro Ala Arg Glu Ser Asn Val Asn Phe Gln Glu
    370                 375                 380

Asp Gly Ile His Trp Tyr Ser Asn Met Leu Phe His Ile Gly Ser Trp
385                 390                 395                 400

Leu Leu Asp Arg Asp Ser Phe His Pro Leu Gly Ile Leu His Leu Ser
                405                 410                 415
```

<210> 19
<211> 1416
<212> DNA
<213> Drosophila HH

<220>
<221> CDS
<222> (1)..(1413)

<400> 19

```
atg gat aac cac agc tca gtg cct tgg gcc agt gcc gcc agt gtc acc   48
Met Asp Asn His Ser Ser Val Pro Trp Ala Ser Ala Ala Ser Val Thr
  1               5                  10                  15
```

```
tgt ctc tcc ctg gga tgc caa atg cca cag ttc cag ttc cag ttc cag   96
Cys Leu Ser Leu Gly Cys Gln Met Pro Gln Phe Gln Phe Gln Phe Gln
             20                  25                  30

ctc caa atc cgc agc gag ctc cat ctc cgc aag ccc gca aga aga acg   144
Leu Gln Ile Arg Ser Glu Leu His Leu Arg Lys Pro Ala Arg Arg Thr
         35                  40                  45

caa acg atg cgc cac att gcg cat acg cag cgt tgc ctc agc agg ctg   192
Gln Thr Met Arg His Ile Ala His Thr Gln Arg Cys Leu Ser Arg Leu
     50                  55                  60

acc tct ctg gtg gcc ctg ctg ctg atc gtc ttg ccg atg gtc ttt agc   240
Thr Ser Leu Val Ala Leu Leu Leu Ile Val Leu Pro Met Val Phe Ser
 65                  70                  75                  80

ccg gct cac agc tgc ggt cct ggc cga gga ttg ggt cgt cat agg gcg   288
Pro Ala His Ser Cys Gly Pro Gly Arg Gly Leu Gly Arg His Arg Ala
                 85                  90                  95

cgc aac ctg tat ccg ctg gtc ctc aag cag aca att ccc aat cta tcc   336
Arg Asn Leu Tyr Pro Leu Val Leu Lys Gln Thr Ile Pro Asn Leu Ser
            100                 105                 110

gag tac acg aac agc gcc tcc gga cct ctg gag ggt gtg atc cgt cgg   384
Glu Tyr Thr Asn Ser Ala Ser Gly Pro Leu Glu Gly Val Ile Arg Arg
        115                 120                 125

gat tcg ccc aaa ttc aag gac ctc gtg ccc aac tac aac agg gac atc   432
Asp Ser Pro Lys Phe Lys Asp Leu Val Pro Asn Tyr Asn Arg Asp Ile
    130                 135                 140

ctt ttc cgt gac gag gaa ggc acc gga gcg gat ggc ttg atg agc aag   480
Leu Phe Arg Asp Glu Glu Gly Thr Gly Ala Asp Gly Leu Met Ser Lys
145                 150                 155                 160

cgc tgc aag gag aag cta aac gtg ctg gcc tac tcg gtg atg aac gaa   528
Arg Cys Lys Glu Lys Leu Asn Val Leu Ala Tyr Ser Val Met Asn Glu
                165                 170                 175

tgg ccc ggc atc cgg ctg ctg gtc acc gag agc tgg gac gag gac tac   576
Trp Pro Gly Ile Arg Leu Leu Val Thr Glu Ser Trp Asp Glu Asp Tyr
            180                 185                 190

cat cac ggc cag gag tcg ctc cac tac gag ggc cga gcg gtg acc att   624
His His Gly Gln Glu Ser Leu His Tyr Glu Gly Arg Ala Val Thr Ile
        195                 200                 205

gcc acc tcc gat cgc gac cag tcc aaa tac ggc atg ctc gct cgc ctg   672
Ala Thr Ser Asp Arg Asp Gln Ser Lys Tyr Gly Met Leu Ala Arg Leu
    210                 215                 220

gcc gtc gag gct gga ttc gat tgg gtc tcc tac gtc agc agg cgc cac   720
Ala Val Glu Ala Gly Phe Asp Trp Val Ser Tyr Val Ser Arg Arg His
225                 230                 235                 240
```

```
atc tac tgc tcc gtc aag tca gat tcg tcg atc agt tcc cac gtg cac   768
Ile Tyr Cys Ser Val Lys Ser Asp Ser Ser Ile Ser Ser His Val His
                245                 250                 255

ggc tgc ttc acg ccg gag agc aca gcg ctg ctg gag agt gga gtc cgg   816
Gly Cys Phe Thr Pro Glu Ser Thr Ala Leu Leu Glu Ser Gly Val Arg
            260                 265                 270

aag ccg ctc ggc gag ctc tct atc gga gat cgt gtt ttg agc atg acc   864
Lys Pro Leu Gly Glu Leu Ser Ile Gly Asp Arg Val Leu Ser Met Thr
        275                 280                 285

gcc aac gga cag gcc gtc tac agc gaa gtg atc ctc ttc atg gac cgc   912
Ala Asn Gly Gln Ala Val Tyr Ser Glu Val Ile Leu Phe Met Asp Arg
    290                 295                 300

aac ctc gag cag atg caa aac ttt gtg cag ctg cac acg gac ggt gga   960
Asn Leu Glu Gln Met Gln Asn Phe Val Gln Leu His Thr Asp Gly Gly
305                 310                 315                 320

gca gtg ctc acg gtg acg ccg gct cac ctg gtt agc gtt tgg cag ccg   1008
Ala Val Leu Thr Val Thr Pro Ala His Leu Val Ser Val Trp Gln Pro
                325                 330                 335

gag agc cag aag ctc acg ttt gtg ttt gcg cat cgc atc gag gag aag   1056
Glu Ser Gln Lys Leu Thr Phe Val Phe Ala His Arg Ile Glu Glu Lys
            340                 345                 350

aac cag gtg ctc gta cgg gat gtg gag acg ggc gag ctg agg ccc cag   1104
Asn Gln Val Leu Val Arg Asp Val Glu Thr Gly Glu Leu Arg Pro Gln
        355                 360                 365

cga gtg gtc aag ttg ggc agt gtg cgc agt aag ggc gtg gtc gcg ccg   1152
Arg Val Val Lys Leu Gly Ser Val Arg Ser Lys Gly Val Val Ala Pro
    370                 375                 380

ctg acc cgc gag ggc acc att gtg gtc aac tcg gtg gcc gcc agt tgc   1200
Leu Thr Arg Glu Gly Thr Ile Val Val Asn Ser Val Ala Ala Ser Cys
385                 390                 395                 400

tat gcg gtg atc aac agt cag tcg ctg gcc cac tgg gga ctg gct ccc   1248
Tyr Ala Val Ile Asn Ser Gln Ser Leu Ala His Trp Gly Leu Ala Pro
                405                 410                 415

atg cgc ctg ctg tcc acg ctg gag gcg tgg ctg ccc gcc aag gag cag   1296
Met Arg Leu Leu Ser Thr Leu Glu Ala Trp Leu Pro Ala Lys Glu Gln
            420                 425                 430

ttg cac agt tcg ccg aag gtg gtg agc tcg gcg cag cag cag aat ggc   1344
Leu His Ser Ser Pro Lys Val Val Ser Ser Ala Gln Gln Gln Asn Gly
        435                 440                 445

atc cat tgg tat gcc aat gcg ctc tac aag gtc aag gac tac gtg ctg   1392
Ile His Trp Tyr Ala Asn Ala Leu Tyr Lys Val Lys Asp Tyr Val Leu
    450                 455                 460

ccg cag agc tgg cgc cac gat tga                                  1416
```

```
Pro Gln Ser Trp Arg His Asp
465                 470


<210> 20
<211> 471
<212> PRT
<213> Drosophila HH

<400> 20
Met Asp Asn His Ser Ser Val Pro Trp Ala Ser Ala Ala Ser Val Thr
  1               5                  10                  15

Cys Leu Ser Leu Gly Cys Gln Met Pro Gln Phe Gln Phe Gln Phe Gln
             20                  25                  30

Leu Gln Ile Arg Ser Glu Leu His Leu Arg Lys Pro Ala Arg Arg Thr
         35                  40                  45

Gln Thr Met Arg His Ile Ala His Thr Gln Arg Cys Leu Ser Arg Leu
     50                  55                  60

Thr Ser Leu Val Ala Leu Leu Leu Ile Val Leu Pro Met Val Phe Ser
 65                  70                  75                  80

Pro Ala His Ser Cys Gly Pro Gly Arg Gly Leu Gly Arg His Arg Ala
                 85                  90                  95

Arg Asn Leu Tyr Pro Leu Val Leu Lys Gln Thr Ile Pro Asn Leu Ser
            100                 105                 110

Glu Tyr Thr Asn Ser Ala Ser Gly Pro Leu Glu Gly Val Ile Arg Arg
        115                 120                 125

Asp Ser Pro Lys Phe Lys Asp Leu Val Pro Asn Tyr Asn Arg Asp Ile
    130                 135                 140

Leu Phe Arg Asp Glu Glu Gly Thr Gly Ala Asp Gly Leu Met Ser Lys
145                 150                 155                 160

Arg Cys Lys Glu Lys Leu Asn Val Leu Ala Tyr Ser Val Met Asn Glu
                165                 170                 175

Trp Pro Gly Ile Arg Leu Leu Val Thr Glu Ser Trp Asp Glu Asp Tyr
            180                 185                 190

His His Gly Gln Glu Ser Leu His Tyr Glu Gly Arg Ala Val Thr Ile
        195                 200                 205

Ala Thr Ser Asp Arg Asp Gln Ser Lys Tyr Gly Met Leu Ala Arg Leu
    210                 215                 220

Ala Val Glu Ala Gly Phe Asp Trp Val Ser Tyr Val Ser Arg Arg His
225                 230                 235                 240

Ile Tyr Cys Ser Val Lys Ser Asp Ser Ser Ile Ser Ser His Val His
                245                 250                 255
```

```
Gly Cys Phe Thr Pro Glu Ser Thr Ala Leu Leu Glu Ser Gly Val Arg
            260                 265                 270

Lys Pro Leu Gly Glu Leu Ser Ile Gly Asp Arg Val Leu Ser Met Thr
        275                 280                 285

Ala Asn Gly Gln Ala Val Tyr Ser Glu Val Ile Leu Phe Met Asp Arg
    290                 295                 300

Asn Leu Glu Gln Met Gln Asn Phe Val Gln Leu His Thr Asp Gly Gly
305                 310                 315                 320

Ala Val Leu Thr Val Thr Pro Ala His Leu Val Ser Val Trp Gln Pro
                325                 330                 335

Glu Ser Gln Lys Leu Thr Phe Val Phe Ala His Arg Ile Glu Glu Lys
            340                 345                 350

Asn Gln Val Leu Val Arg Asp Val Glu Thr Gly Glu Leu Arg Pro Gln
        355                 360                 365

Arg Val Val Lys Leu Gly Ser Val Arg Ser Lys Gly Val Val Ala Pro
    370                 375                 380

Leu Thr Arg Glu Gly Thr Ile Val Val Asn Ser Val Ala Ala Ser Cys
385                 390                 395                 400

Tyr Ala Val Ile Asn Ser Gln Ser Leu Ala His Trp Gly Leu Ala Pro
                405                 410                 415

Met Arg Leu Leu Ser Thr Leu Glu Ala Trp Leu Pro Ala Lys Glu Gln
            420                 425                 430

Leu His Ser Ser Pro Lys Val Val Ser Ser Ala Gln Gln Gln Asn Gly
        435                 440                 445

Ile His Trp Tyr Ala Asn Ala Leu Tyr Lys Val Lys Asp Tyr Val Leu
    450                 455                 460

Pro Gln Ser Trp Arg His Asp
465                 470
```

<210> 21
<211> 221
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: degenerate polypeptide sequence

<220>
<223> Xaa(7) represents Gly, Ala, Val, Leu, Ile, Phe, Tyr or Trp; Xaa(9) represents Arg, His or Lys; Xaa(44) represents Gly, Ala, Val, Leu, Ile, Ser or Thr; Xaa(85) represents Gly,

Ala, Val, Leu, Ile, Ser or Thr; Xaa(93) represents Lys, Arg, His, Asn or Gln; Xaa(98) represents Lys, Arg or His; Xaa(112) represents Ser, Thr, Tyr, Trp or Phe; Xaa(132) represents Lys, Arg or His; Xaa(137) represents Met, Cys, Ser or Thr; Xaa(139) represents Gly, Ala, Val, Leu, Ile, Ser or Thr; Xaa(181) represents Leu, Val, Met, Thr or Ser; Xaa(183) represents His, Phe, Tyr, Ser, Thr, Met or Cys; Xaa(185) represents Gln, Asn, Glu, or Asp; Xaa(186) represents His, Phe, Tyr, Thr, Gln, Asn, Glu or Asp; Xaa(189) represents Gln, Asn, Glu, Asp, Thr, Ser, Met or Cys; Xaa(191) represents Ala, Gly, Cys, Leu, Val or Met; Xaa(196) represents Arg, Lys, Met, Ile, Asn, Asp, Glu, Gln, Ser, Thr or Cys; Xaa(200) represents Arg, Lys, Met or Ile; Xaa(206) represents Ala, Gly, Cys, Asp, Glu, Gln, Asn, Ser, Thr or Met; Xaa(207) represents Ala, Gly, Cys, Asp, Asn, Glu or Gln; Xaa(209) represents Arg, Lys, Met, Ile, Asn, Asp, Glu or Gln; Xaa(211) represents Leu, Val, Met or Ile; Xaa(212) represents Phe, Tyr, Thr, His or Trp; Xaa(216) represents Ile, Val, Leu or Met; Xaa(217) represents Met, Cys, Ile, Leu, Val, Thr or Ser; Xaa(219) represents Leu, Val, Met, Thr or Ser. In an even more expansive library, each Xaa can be selected from any amino acid.

<400> 21

```
Cys Gly Pro Gly Arg Gly Xaa Gly Xaa Arg Arg His Pro Lys Lys Leu
  1               5                  10                  15

Thr Pro Leu Ala Tyr Lys Gln Phe Ile Pro Asn Val Ala Glu Lys Thr
             20                  25                  30

Leu Gly Ala Ser Gly Arg Tyr Glu Gly Lys Ile Xaa Arg Asn Ser Glu
         35                  40                  45

Arg Phe Lys Glu Leu Thr Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys
     50                  55                  60

Asp Glu Glu Asn Thr Gly Ala Asp Arg Leu Met Thr Gln Arg Cys Lys
 65                  70                  75                  80

Asp Lys Leu Asn Xaa Leu Ala Ile Ser Val Met Asn Xaa Trp Pro Gly
                 85                  90                  95

Val Xaa Leu Arg Val Thr Glu Gly Trp Asp Glu Asp Gly His His Xaa
            100                 105                 110

Glu Glu Ser Leu His Tyr Glu Gly Arg Ala Val Asp Ile Thr Thr Ser
        115                 120                 125

Asp Arg Asp Xaa Ser Lys Tyr Gly Xaa Leu Xaa Arg Leu Ala Val Glu
    130                 135                 140

Ala Gly Phe Asp Trp Val Tyr Tyr Glu Ser Lys Ala His Ile His Cys
145                 150                 155                 160

Ser Val Lys Ala Glu Asn Ser Val Ala Ala Lys Ser Gly Gly Cys Phe
                165                 170                 175

Pro Gly Ser Ala Xaa Val Xaa Leu Xaa Xaa Gly Gly Xaa Lys Xaa Val
            180                 185                 190
```

Lys Asp Leu Xaa Pro Gly Asp Xaa Val Leu Ala Ala Asp Xaa Xaa Gly
195 200 205

Xaa Leu Xaa Xaa Ser Asp Phe Xaa Xaa Phe Xaa Asp Arg
210 215 220

<210> 22
<211> 167
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: degenerate polypeptide sequence

<220>
<223> Xaa(7) represents Gly, Ala, Val, Leu, Ile, Pro, Phe or Tyr; Xaa(8) represents Gly, Ala, Val, Leu or Ile; Xaa(9) represents Gly, Ala, Val, Leu, Ile, Lys, His or Arg; Xaa(12) represents Lys, Arg or His; Xaa(13) represents Phe, Trp, Tyr or an amino acid gap; Xaa(14) represents Gly, Ala, Val, Leu, Ile or an amino acid gap; Xaa(17) represents Asn, Gln, His, Arg or Lys; Xaa(19) represents Gly, Ala, Val, Leu, Ile, Ser or Thr; Xaa(22) represents Gly, Ala, Val, Leu, Ile, Ser or Thr; Xaa(27) represents Gly, Ala, Val, Leu, Ile, Ser or Thr; Xaa(29) represents Ser, Thr, Gln or Asn; Xaa(30) represents Met, Cys, Gly, Ala, Val, Leu, Ile, Ser or Thr; Xaa(31) represents Gly, Ala, Val, Leu, Ile or Pro; Xaa(33) represents Arg, His or Lys; Xaa(40) represents Gly, Ala, Val, Leu, Ile, Pro, Arg, His or Lys; Xaa(41) represents Gly, Ala, Val, Leu, Ile, Phe or Tyr; Xaa(44) represents Arg, His or Lys; Xaa(45) represents Gly, Ala, Val, Leu, Ile, Ser or Thr; Xaa(46) represents Thr or Ser; Xaa(48) represents Gly, Ala, Val, Leu, Ile, Asn or Gln; Xaa(53) represents Arg, His or Lys; Xaa(54) represents Asp or Glu; Xaa(71) represents Ser or Thr; Xaa(79) represents Glu, Asp, Gln or Asn; Xaa(83) represents Glu or Asp; Xaa(84) represents Arg, His or Lys; Xaa(85) represents Gly, Ala, Val, Leu or Ile; Xaa(87) represents Gly, Ala, Val, Leu, Ile, Thr or Ser; Xaa(95) represents Met, Cys, Gln, Asn, Arg, Lys or His; Xaa(100) represents Arg, His or Lys; Xaa(107) represents Trp, Phe, Tyr, Arg, His or Lys; Xaa(114) represents Gly, Ala, Val, Leu, Ile, Ser, Thr, Tyr or Phe; Xaa(115) represents Gln, Asn, Asp or Glu; Xaa(116) represents Asp or Glu; Xaa(125) represents Gly, Ala, Val, Leu, or Ile; Xaa(134) represents Arg, His or Lys; Xaa(135) represents Asn, Gln, Thr or Ser; Xaa(139) represents Gly, Ala, Val, Leu, Ile, Ser, Thr, Met or Cys; Xaa(141) represents Gly, Ala, Val, Leu, Ile, Thr or Ser; Xaa(157) represents Arg, His or Lys; Xaa(158) represents Asn, Gln, Gly, Ala, Val, Leu or Ile; Xaa(160) represents Gly, Ala, Val, Leu or Ile; Xaa(162) represents Gly, Ala, Val, Leu, Ile, Ser, Thr or Cys; Xaa(166) represents Gly, Ala, Val, Leu, Ile, Thr or Ser; and Xaa(167) represents Asp or Glu.

<400> 22
Cys Gly Pro Gly Arg Gly Xaa Xaa Xaa Arg Arg Xaa Xaa Xaa Pro Lys
1 5 10 15

Xaa Leu Xaa Pro Leu Xaa Tyr Lys Gln Phe Xaa Pro Xaa Xaa Xaa Glu
20 25 30

Xaa Thr Leu Gly Ala Ser Gly Xaa Xaa Glu Gly Xaa Xaa Xaa Arg Xaa
35 40 45

Ser Glu Arg Phe Xaa Xaa Leu Thr Pro Asn Tyr Asn Pro Asp Ile Ile
50 55 60

Phe Lys Asp Glu Glu Asn Xaa Gly Ala Asp Arg Leu Met Thr Xaa Arg
65 70 75 80

Cys Lys Xaa Xaa Xaa Asn Xaa Leu Ala Ile Ser Val Met Asn Xaa Trp
85 90 95

Pro Gly Val Xaa Leu Arg Val Thr Glu Gly Xaa Asp Glu Asp Gly His
100 105 110

His Xaa Xaa Xaa Ser Leu His Tyr Glu Gly Arg Ala Xaa Asp Ile Thr
115 120 125

Thr Ser Asp Arg Asp Xaa Xaa Lys Tyr Gly Xaa Leu Xaa Arg Leu Ala
130 135 140

Val Glu Ala Gly Phe Asp Trp Val Tyr Tyr Glu Ser Xaa Xaa His Xaa
145 150 155 160

His Xaa Ser Val Lys Xaa Xaa
165

<210> 23
<211> 74
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: primer

<400> 23
gcgcgcttcg aagcgaggca gccagcgagg gagagagcga gcgggcgagc cggagcgagg 60

aaatcgatgc gcgc 74

<210> 24
<211> 74
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: primer

<400> 24
gcgcgcagat ctgggaaagc gcaagagaga gcgcacacgc acacacccgc cgcgcgcact 60

cgggatccgc gcgc 74

<210> 25
<211> 996
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: gene
activation construct

<400> 25
cgaagcgagg cagccagcga gggagagagc gagcgggcga gccggagcga ggaaatcgaa 60

ggttcgaatc cttcccccac caccatcact ttcaaaagtc cgaaagaatc tgctccctgc 120

ttgtgtgttg gaggtcgctg agtagtgcgc gagtaaaatt taagctacaa caaggcaagg 180

cttgaccgac aattgcatga agaatctgct tagggttagg cgttttgcgc tgcttcgcga 240

tgtacgggcc agatatacgc gttgacattg attattgact agttattaat agtaatcaat 300

tacggggtca ttagttcata gcccatatat ggagttccgc gttacataac ttacggtaaa 360

tggcccgcct ggctgaccgc ccaacgaccc ccgcccattg acgtcaataa tgacgtatgt 420

tcccatagta acgccaatag ggactttcca ttgacgtcaa tgggtggact atttacggta 480

aactgcccac ttggcagtac atcaagtgta tcatatgcca agtacgcccc ctattgacgt 540

caatgacggt aaatggcccg cctggcatta tgcccagtac atgaccttat gggactttcc 600

tacttggcag tacatctacg tattagtcat cgctattacc atggtgatgc ggttttggca 660

gtacatcaat gggcgtggat agcggtttga ctcacgggga tttccaagtc tccaccccat 720

tgacgtcaat gggagtttgt tttggcacca aaatcaacgg gactttccaa aatgtcgtaa 780

caactccgcc ccattgacgc aaatgggcgg taggcgtgta cggtgggagg tctatataag 840

cagagctctc tggctaacta gagaacccac tgcttactgg cttatcgaaa ttaatacgac 900

tcactatagg gagacccaag cttggtaccg agctcggatc gatctgggaa agcgcaagag 960

agagcgcaca cgcacacacc cgccgcgcgc actcgg 996

<210> 26
<211> 26
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: antisense
construct

<400> 26
gtcctggcgc cgccgccgcc gtcgcc 26

<210> 27
<211> 26
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: antisense construct

<400> 27
ttccgatgac cggcctttcg cggtga 26

<210> 28
<211> 26
<212> DNA
<213> Artificial Sequence

a2 cont

<220>
<223> Description of Artificial Sequence: antisense construct

<400> 28
gtgcacggaa aggtgcaggc cacact 26